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SURGICAL TREATMENT OF OTOSCLEROSIS

A Preliminary Report on an Improved Fenestration Technic

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A PRACTICAL one stage operative technic for the improvement of hearing in otosclerosis first became available in 1938 when Lempert [1] introduced the fenestration operation. From a small beginning, beset with many failures, the operation has developed to a highly refined procedure which has been carried out on several thousands of patients suffering from otosclerosis, with varying but with generally increasing success.

The evolutionary development of the fenestration operation has taken several directions. In one of these directions, pursued at the Wesley Memorial Hospital and Northwestern University Medical School as a result of research studies carried out during the last four years on the monkey, a new fenestration technic has developed which will be described in the present communication, with the results thus far observed.

Whether or not the new fenestration technic represents an improvement over other technics will be determined by a comparison of the hearing results in a sufficiently large series of cases observed over a sufficiently long period.[2]

Recent studies of the permanence of the hearing improvement following the fenestration operation have been made at Northwestern University, based on experimental and on clinical observations. The experimental studies showed that in the monkey osteogenesis tending to close the fistula is most active during the first three postoperative months. Thereafter the osteogenesis at the fistula gradually subsides and finally ceases. Allowing for considerable differences between ears, one may state that in the monkey active osteogenesis, as a rule, has practically ceased at the fistula about four months after the fenestration operation.

Read before the Buffalo Otolaryngological Society, March 27, 1946.

1. Lempert, J.: Improvement of Hearing in Cases of Otosclerosis: New One-Stage Surgical Technic, Arch. Otolaryng. **28**:42-97 (July) 1938.

2. Shambaugh, G. E., Jr.: Surgical Treatment of Otosclerosis: Comparative Analysis of Results Using Different Technics, Ann. Otol., Rhin. & Laryng. **51**: 817 (Sept.) 1942.

The clinical studies of the permanence of the hearing improvement were made in 800 consecutive cases in which the fenestration operation was performed and the hearing followed with repeated audiometric determinations over a period of seven years.[3] It was found that loss of the hearing improvement had occurred in 51 cases. In 32 of these the operation was repeated and bony closure of the labyrinthine fistula was observed in every instance. In some of these cases there was still a positive reaction with the fistula test at the time of reoperation, due to the fact that there was a band of fibrous tissue extending through a tiny opening in the new bone—too small to permit the transmission of sound vibrations. The fistula test, therefore cannot be used to judge the functional patency of the fistula to sound; this can be determined only by audiometric tests showing a maintained hearing improvement.

Of the 51 cases in which the hearing improvement was lost, owing presumably to bony closure, the majority (82 per cent) were cases in which the fistula closed within the first year after operation. A few were cases in which the fistula closed during the second postoperative year, but only in 1 of the cases had it closed later than two years after operation. The conclusion was reached that osteogenesis tending to close the fistula after the fenestration operation in the human patient usually ceases by the end of the first postoperative year and has practically always ceased by the end of the second postoperative year. A hearing improvement maintained for more than two years after the fenestration operation may be regarded as an "almost certainly permanent" result.[4]

The validity of the statement that the two year hearing result may be considered the permanent result of the fenestration operation is borne out by the hearing tests made five and six years after operation. Without exception, a hearing improvement in the fenestrated ear maintained for two years after operation has been maintained without further loss for five and six years in 31 cases followed for this length of time (table 1; fig. 1).

It is vital to the further development of the fenestration operation that its results be made accessible so that the merits of any new technic may be judged in comparison with those of other technics. To this end it is our established policy at Northwestern University to make available for all who wish to study and examine them the audiometric data on every case of fenestration.

These data are summarized on a "fenestration score board" at the Wesley Memorial Hospital. The results of each day's audiometric tests

3. Shambaugh, G. E., Jr.: Fenestration Operation: A Clinical Study of the Permanence of Its Results, Quart. Bull. Northwestern Univ. M. School **19**:259, 1945.

4. This refers only to the hearing defect due to otosclerotic ankylosis of the stapes and not to subsequent losses due to otosclerotic degeneration of the nerve or to senile degeneration of the nerve or other unrelated processes.

of patients operated on are incorporated that afternoon on the score board, so that it is always strictly up to date. To facilitate an appraisal of the results, colored indicators are used to call attention to the patients who failed to obtain an improvement, to those whose hearing was made worse and to those who lost their improvement owing to closure of the fistula. All otologists interested in examining the results of the fenestration operation are invited to study this score board which includes more than 1,000 consecutive fenestration operations performed by us and followed over a period of nearly eight years.

TABLE 1.—*Hearing Improvement Two and Five or More Years After Fenestration Operation*

(Continuous Irrigation and Use of Microscope in All Except Case 1)

Case	Improvement Two Years After Operation in Decibels for Speech Frequencies	Improvement Five to Six Years After Operation in Decibels for Speech Frequencies	Hearing Loss for Speech Frequencies Five to Six Years After operation
1 (Revision)	+34	+32 (5½ Years)	35
8	+22	+22 (5 Years)	25
12	+19	+25 (5 Years)	42
14	+22	+20 (6 Years)	37
17	+29	+29 (6 Years)	28
19	+25	+22 (5 Years)	38
22	+26	+21 (6 Years)	47
23	+28	+26 (5 Years)	30
24	+15	+19 (5½ Years)	28
26	+25	+29 (5 Years)	33
28	+24	+32 (5 Years)	30
30	+32	+29 (5½ Years)	28
32 (Revision)	+30	+31 (5 Years)	31
33	+16	+23 (5½ Years)	23
34	+30	+23 (5½ Years)	27
35	+30	+28 (5½ Years)	25
36	+21	+23 (5 Years)	38
38	+22	+22 (5 Years)	20
41	+26	+31 (5 Years)	38
44	+23	+28 (5½ Years)	25
46	+32	+27 (5½ Years)	32
47	+26	+28 (5½ Years)	30
48	+30	+36 (5 Years)	32
51	+18	+18 (5 Years)	42
52	+26	+29 (5 Years)	27
54	+30	+32 (5 Years)	40
56	+13	+17 (5 Years)	38
57	+28	+35 (5 Years)	35
59	+24	+30 (5 Years)	20
63	+36	+37 (5 Years)	30
66	+29	+27 (5 Years)	27

Although the hearing failed to reach the 30 decibel level for the speech frequencies in 16 of the 31 patients, not one has used a hearing aid at any time since operation. The patient with the poorest result (case 22) now has a 47 decibel loss for the speech frequencies (512, 1024 and 2048 cycles).

THE NEW FENESTRATION TECHNIC

In no way is the new fenestration technic developed at Northwestern University presented as a finished or final technic, for the fenestration operation is still in its infancy and we, and others doing it, are constantly

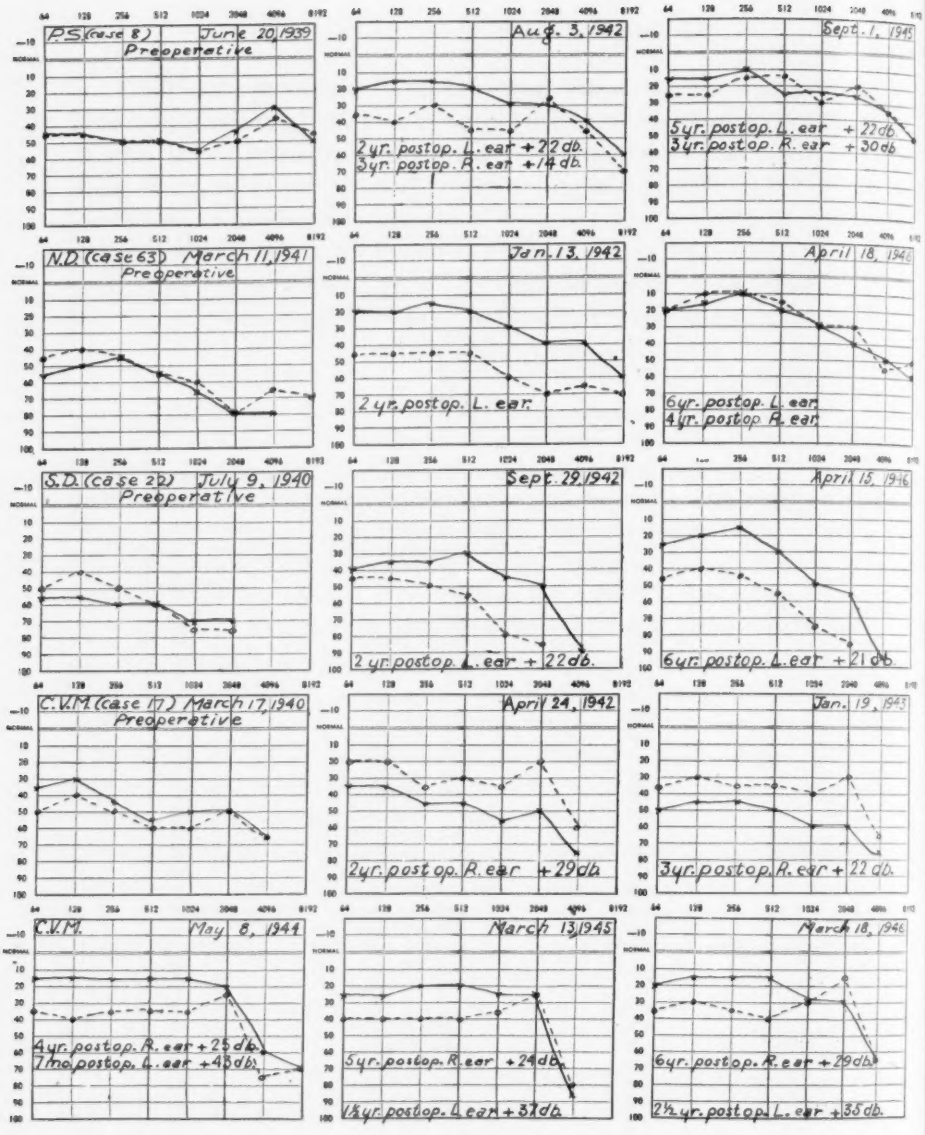
P.S. (case 8) June 20, 1939
Preoperative
Aug. 3, 1942
2 yr. postop. L. ear + 22 db.
3 yr. postop. R. ear + 14 db.
Sept. 1, 1941
5 yr. postop. L. ear + 22 db.
3 yr. postop. R. ear + 30 db.
N.D. (case 63) March 11, 1941
Preoperative
Jan. 13, 1942
2 yr. postop. L. ear.
April 18, 1946
6 yr. postop. L. ear
4 yr. postop. R. ear
S.D. (case 22) July 9, 1940
Preoperative
Sept. 29, 1942
2 yr. postop. L. ear + 22 db.
April 15, 1946
6 yr. postop. L. ear + 21 db.
C.V.M. (case 17) March 17, 1940
Preoperative
April 24, 1942
2 yr. postop. R. ear + 29 db.
Jan. 19, 1943
3 yr. postop. R. ear + 22 db.
C.V.M.
May 8, 1944
4 yr. postop. R. ear + 25 db.
7 mo. postop. L. ear + 43 db.
March 13, 1945
5 yr. postop. R. ear + 24 db.
1½ yr. postop. L. ear + 37 db.
March 18, 1946
6 yr. postop. R. ear + 29 db.
2½ yr. postop. L. ear + 35 db.

Fig. 1.—Four series of audiograms showing that a hearing improvement which is still present two years after the fenestration operation is a permanent improvement. The small numbers at the top of each audiogram represent double vibrations per second (tonal frequencies); those at the left, decibels. Hearing for air-conducted tones is represented in the curves (right ear, circles; left ear, crosses).

In this figure patients P. S., N. D. and S. D. are represented by three audiograms each, arranged from left to right, and patient C. V. M. by six audiograms. The initials of the patient and the dates of the audiometric tests are given near the top in each set of audiograms.

The decibel gains stated below the curves are gains in the speech range.

In patients P. S. and N. D. the hearing improvement of the right ear was maintained without loss for periods of two to six years.

Patient S. D. had used an electrical hearing aid for eight years before operation. Since the operation he has not needed an aid despite a loss of 47 decibels for the speech frequencies. The audiograms show his hearing improvement maintained when tested two years after operation and again six years after operation.

In patient C. V. M. a hearing improvement was shown two years and six years after operation.

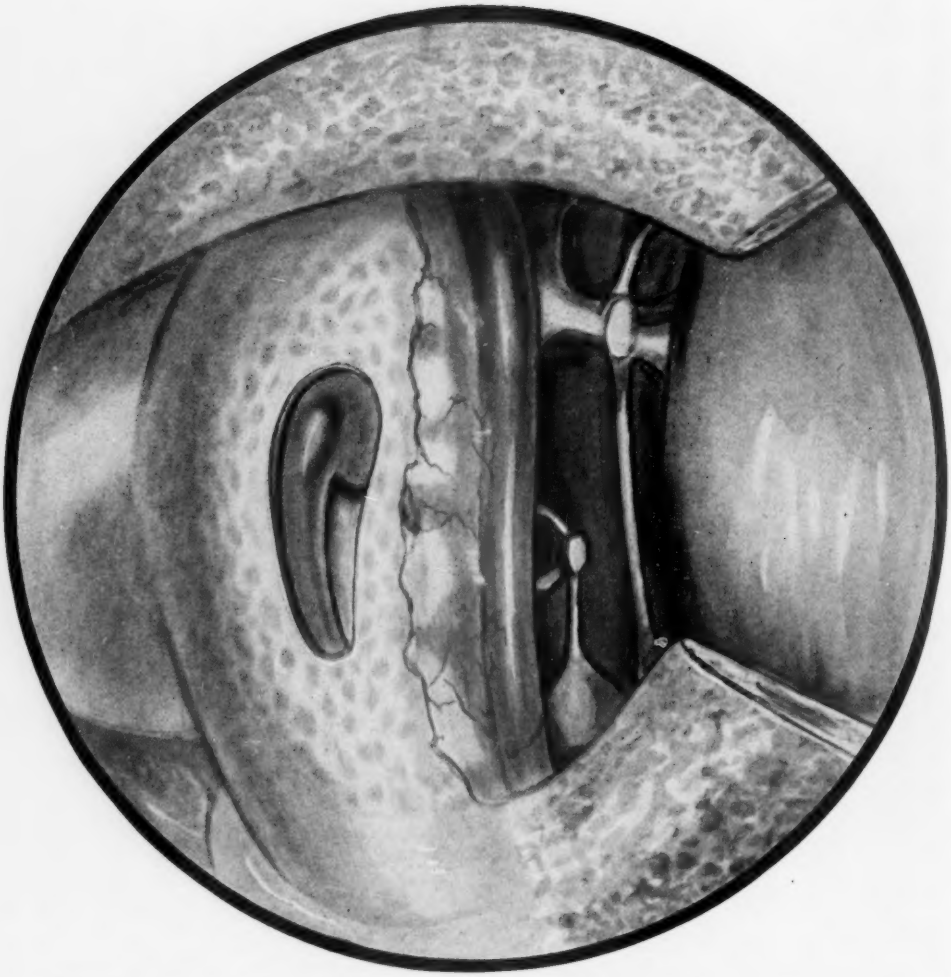

Fig. 2.—Completed fistula (human) on the lateral surface of the horizontal semicircular canal as viewed through the operating microscope. Observe the granular-appearing enchondral layer of the capsule, exposed widely around the fistula, and the middle ear mucosa that nearly reaches the fistula.

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looking for further improvements. Nevertheless, the results obtained with the technic in its present stage of development are sufficiently encouraging to warrant the publication of this preliminary report.

The new fenestration technic embodies several major changes and a number of minor changes of technics developed elsewhere. The minor changes decrease the number of postoperative treatments and increase the comfort and the safety of the operation for the patient. The major changes are believed to improve the permanent hearing results of the operation, and fall into three categories: features to decrease the frequency of bony closure, features to enhance the average decibel gain and features to lessen postoperative labyrinthitis.

Features Designed to Decrease the Frequency of Bony Closure.—As a result of experimental observations made on the monkey, described in detail in another communication,[5] certain factors that influence osteogenesis after the fenestration operation have been brought out. The application of this new knowledge to the fenestration operation has reduced the incidence of bony closure with loss of the hearing improvement to 5 per cent of operations followed for more than two years (tables 2 and 3).

The following major changes of technic have been introduced to prevent osteogenesis:

1. Enchondralization of the fistula. After the otic capsule of the semicircular canals has been skeletonized as described by Lempert, the constant irrigation apparatus and the microscope are employed to improve the visibility of the operative field. With a diamond-cutting burr, the periosteal layer of the otic capsule is removed from the lateral, anterior and superior surfaces of the horizontal semicircular canal, leaving a thin shell of the enchondral layer exposed widely beyond the gray line that denotes the site of the future labyrinthine fistula. The enchondral bone may be recognized through the microscope by its more yellowish, coarsely granular surface suggesting tapioca or pineapple ice cream, as compared with the periosteal bone, which is more homogeneous and whiter, resembling frosted glass or vanilla ice cream (fig. 2).

The observations made on the monkey showed that enchondral bone responds to trauma less readily with new bone formation than does periosteal bone (fig. 3). Enchondralization of the fistula has virtually eliminated bony closure due to osteogenesis from outside the fistula, as we have observed in fistulas made by this technic that subsequently closed and were reopened.

5. Shambaugh, G. E., Jr.: Factors Influencing Osteogenesis Following the Fenestration Operation: Observations on the Monkey, to be published.

2. Instantaneous removal of bone dust from the fistula. The stimulating effect on osteogenesis of bone particles and bone dust created by the dental burr cannot be overemphasized as a cause of the bony closing of the fistula after the fenestration operation. The instantaneous and continuous flushing away of bone dust by means of a steady flow of Ringer's solution has been a major factor in decreasing the incidence of bony closure since it was introduced by one of us.[6] Continuous irrigation by its nature probably provides greater protection of the labyrinth than any form of intermittent irrigation (fig. 4).

TABLE 2.—*Summary of "Permanent" Hearing Results in 421 Cases in Which Hearing Was Tested Two Years or More After Operation*

Technic	Hearing Never Improved or Worse	Improvement Lost Presumably Because of Closure	Hearing Improved (more than 10 db.) but Initial Gain Partly Lost	Maximum Hearing Improvement Fully Maintained	Total Number of Cases
1. Original Lempert fenestration operation	3 (20%)	8 (54%)	1 (7%)	3 (20%)	15
2. Continuous irrigation added	1 (3½%)	10 (34½%)	2 (7%)	16 (55%)	29
3. Use of microscope and continuous irrigation added	1 (1/2%)	16 (25½%)	6 (9½%)	40 (63½%)	63
4. Modified nov-ovalis fenestration with use of microscope and irrigation	13 (4%)	17 (5%)	6 (2%)	278* (89%)	314

* The average gain for this group is 28.9 decibels.

TABLE 3.—*Breakdown of Cases with Hearing Improvement Fully Maintained*

Technic (see table 2)	Improved 10 to 19 db.	Improved 20 to 29 db.	Improved 30 to 39 db.	Improved more than 40 db.	Total Number of Cases with Improvement Fully Maintained
1	3 (100%)	.. ..	.. ..	.. ..	3 ..
2	.. ..	11 (69%)	5 (31%)	.. ..	16 ..
3	9 (22½%)	13 (32½%)	18 (45%)	.. ..	40 ..
4	47 (17%)	107 (38%)	98 (35%)	26 (10%)	278

3. Avoidance of trauma to the endosteum within the labyrinth. Bone proliferating from the endosteal layer of the otic capsule within the margins of the fistula accounts for the majority of bony closures that we have observed at reoperation since adopting the preceding two features. The experimental observations made on the monkey indicate that the endosteal bone underlying the delicate endosteum lining the labyrinth responds

6. Shambaugh, G. E., Jr.: A Modified Fenestration Technic, Arch. Otolaryng. **36**:23 (July) 1942.

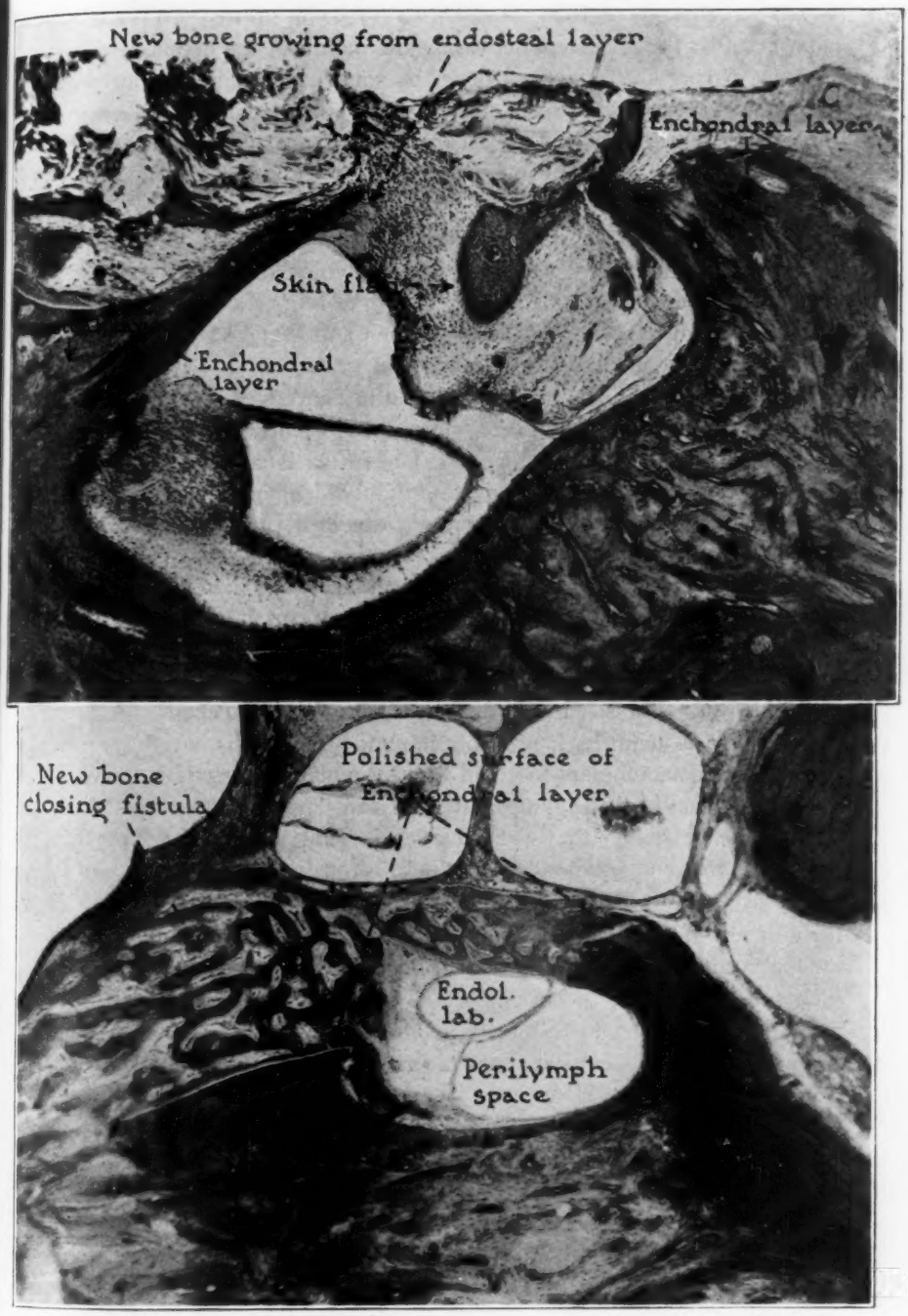

Fig. 3.—Upper: Fistula narrowed by new bone growing from the endosteal layer of the capsule within the margins of the fistula six weeks after operation (monkey). Note the absence of osteogenesis starting from the enchondral layer of the capsule.

Lower: Fistula closed by new bone after it had been covered with fascia instead of skin, two and one-half months after operation (monkey). Note the absence of any osteogenesis originating from the polished surface of the enchondral layer of the capsule.

to any trauma by active osteogenesis (fig. 3, upper part). It is necessary that the endosteum covering the mouth of the fistula, with its adherent particles of endosteal bone, be completely removed, but with scrupulous care to avoid instrumental traumatization of the endosteum lining the labyrinth within the margins of the fistula. This can be accomplished best under adequate magnification with the operating microscope in a field kept immaculately clean by continuous irrigation.[6]

4. Removal of bone particles from the tympanomeatal skin flap. If the periosteal surface of the skin flap is minutely searched with the binocular loupe for embedded and adherent bone particles, a surprising number of such particles can be discovered and removed with fine forceps, a small periosteal elevator and a manicure scissors.

It is unlikely that Shrapnell's membrane covers the fistula as was originally described by Lempert, since this membrane is too small to even reach the fistula in most cases. The fistula is covered rather with the periosteal surface of the tympanomeatal skin flap. Contrary to the prevalent notion, it seems likely that periosteum normally inhibits rather than promotes bone formation. Periosteum and endosteum, alike, consist of a thin layer of dense connective tissue which acts as a limiting membrane. As soon as periosteum or endosteum is removed or damaged, the outer cambium layer of bone begins to proliferate. This view of the function of periosteum is not new; it was advanced as long ago as 1912 by MacEwen,[7] who based it on extensive animal experiments.

While periosteum itself probably inhibits osteogenesis, any bone particles that remain adherent to it will act to stimulate osteogenesis. Unless the under surface of the tympanomeatal skin flap is minutely searched, there is the possibility that when the flap is being placed a bone particle will fall across the fistula and contribute toward its subsequent closure.

5. Taking full advantage of the inhibiting effect of squamous epithelium on osteogenesis. This effect, clearly demonstrated in our monkeys, and observed by otologists in cases of cholesteatoma and by orthopedic surgeons,[8] is an important factor in the successful results occasionally attained by Sourdille's tympanolabyrinthopexy, and more frequently by the Lempert fenestration operation (fig. 3, lower). If full advantage of this effect is to be taken, the stratified squamous epithelium should lie as close to the bone as possible. This is accomplished, first, by thinning the thickened outer portion of the skin flap, which is done by removing the subcutaneous fibrous tissue with iridectomy forceps and manicure scissors. Second, the fistula is made at the top of a rounded mound rather than on the surface of a plain or at the bottom of a depression, so that the skin clings ever more closely to the margins

7. MacEwen, W.: The Growth of Bone, Glasgow, J. MacLehose, 1912.

8. McElvenny, R.: Personal communication to the authors.

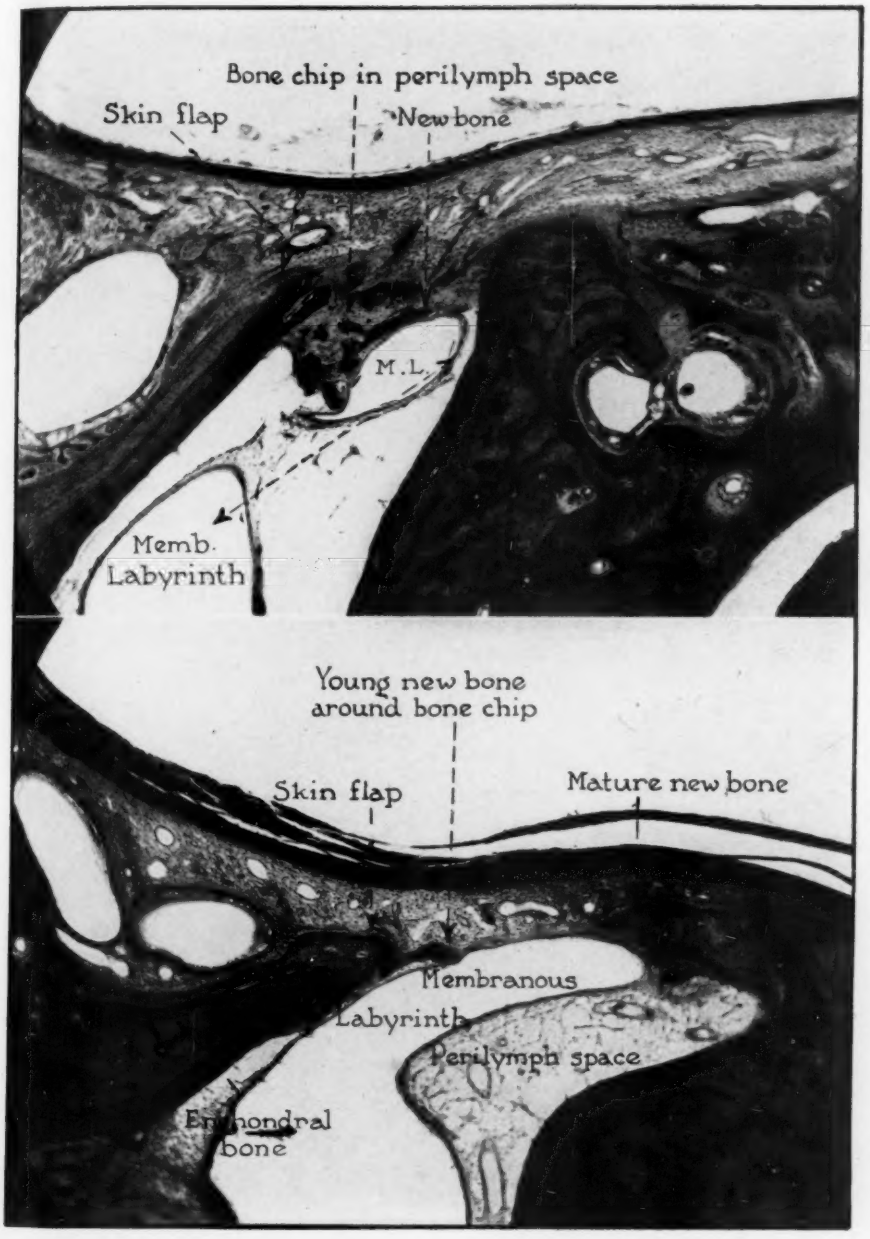

Fig. 4.—Upper: Fistula made without continuous irrigation, bone dust having been removed with a moist cotton applicator, three and one-half months after operation (monkey). Note the bone dust fragments surrounded by new bone completely closing the fistula.

Lower: Osteogenesis occurring around a particle of bone dust three and one-half months after operation (monkey).

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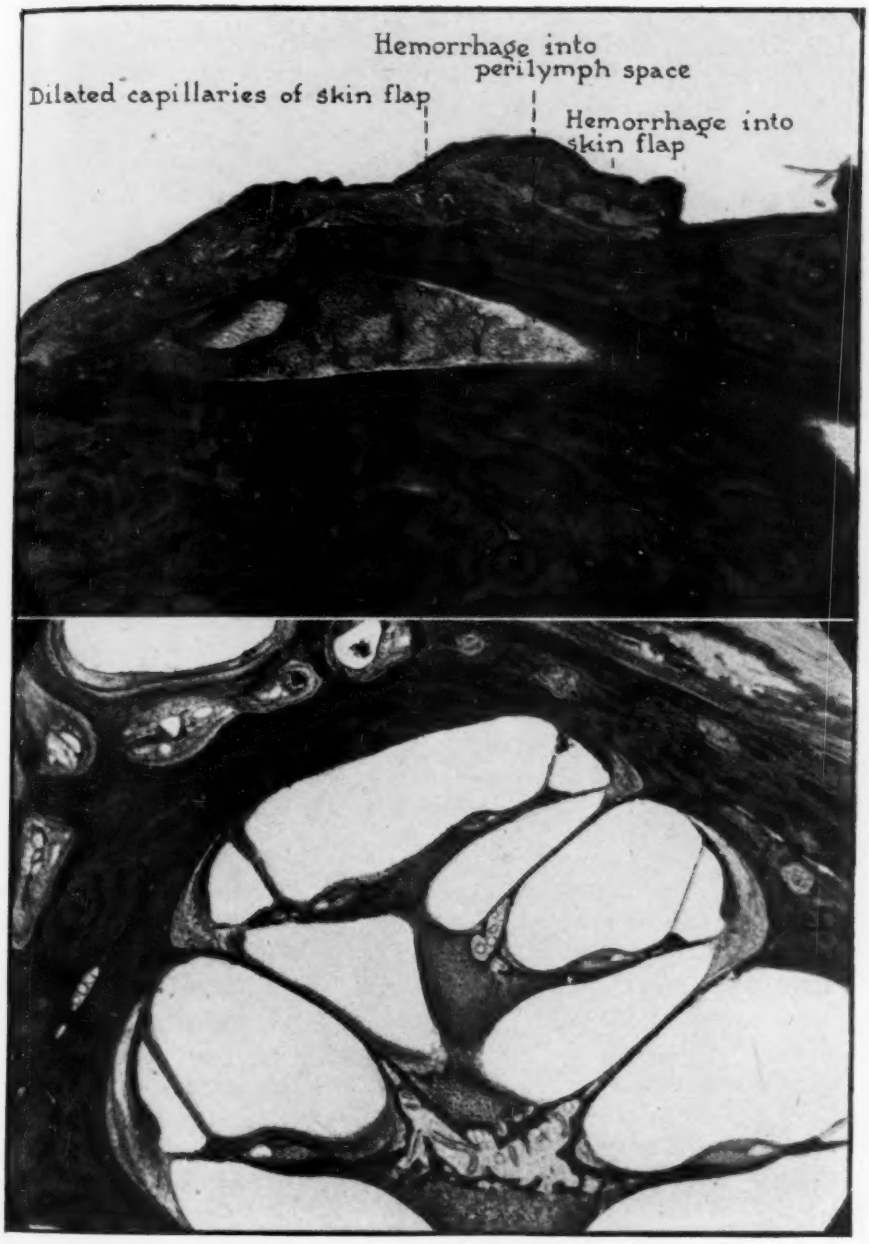

Fig. 5.—Upper: Fistula showing, three days after operation, an inflammatory reaction in the tympanomeatal skin flap with blood in the perilymphatic space of the labyrinth (monkey).

Lower: Cochlea showing blood in the dependent portions of the perilymphatic space one month after operation (monkey). Note the adhesive degeneration of the organ of Corti.

of the fistula as healing and contraction proceed. Third, the very thin skin from the anterior meatal wall is swung around to cover as much of the fistula as possible, rather than the thicker skin from the superior meatal wall. In such cases there can be no question but that the fistula is covered with a periosteum-lined membrane, and some of our best permanent hearing improvements have resulted from this technic.

Features to Enhance the Average Decibel Gain.—The observation has been made by us that patients who have unusually large decibel gains after the fenestration operation frequently exhibit a strongly positive reaction to the fistula test when light pressure is applied to the lower edge of the tense portion of the tympanic membrane, indicating excellent mobility between it and the fistula (fig. 6 [F. W.]). On the other hand, patients with smaller decibel gains frequently exhibit a negative reaction to the fistula test when light pressure is applied to the lower edge of the tympanic membrane, although the reaction to this test is strongly positive at the fistula, suggesting poor mobility between the tympanic membrane and the fistula.

The observation was also made by us that when the tympanic membrane is perforated accidentally during the operation, or as the result of acute otitis media months or years after the operation, the hearing shows little improvement until this perforation is closed by a prosthesis, or heals (fig. 6 [O.A. and A.H.]).

These two observations are evidence that after a successful fenestration operation the patient hears largely by means of sound vibrations carried by the tympanic membrane to the labyrinthine fistula. The following measures to enhance the mobility between the tympanic membrane and the fistula have been incorporated in the new technic:

1. Lateral placement of the fistula. Because of the close proximity of the facial nerve to the nov-ovalis fistula it is easier and it has been customary to place the fistula on the superolateral surface of the ampullated end of the horizontal semicircular canal.[9] The tympanomeatal skin flap must then pass over a vibration-inhibiting mound or ridge of bone before reaching the fistula. In our technic the fistula is placed on the extreme lateral or even the inferolateral surface of the canal and the vibrations of the tympanic membrane reach the fistula without passing over a bony ridge. With the dental finishing burr the bone lying between the fistula and the facial nerve is removed flush with the nerve in its bony canal. This may be accomplished safely without endangering the integrity of the facial nerve, with the improved visualization afforded by the microscope and the constant irrigating apparatus.

9. Lempert, J.: Fenestra Nov-Ovalis: A New Oval Window for the Improvement of Hearing in Cases of Otosclerosis, Arch. Otolaryng. **34**:880 (Nov.) 1941.

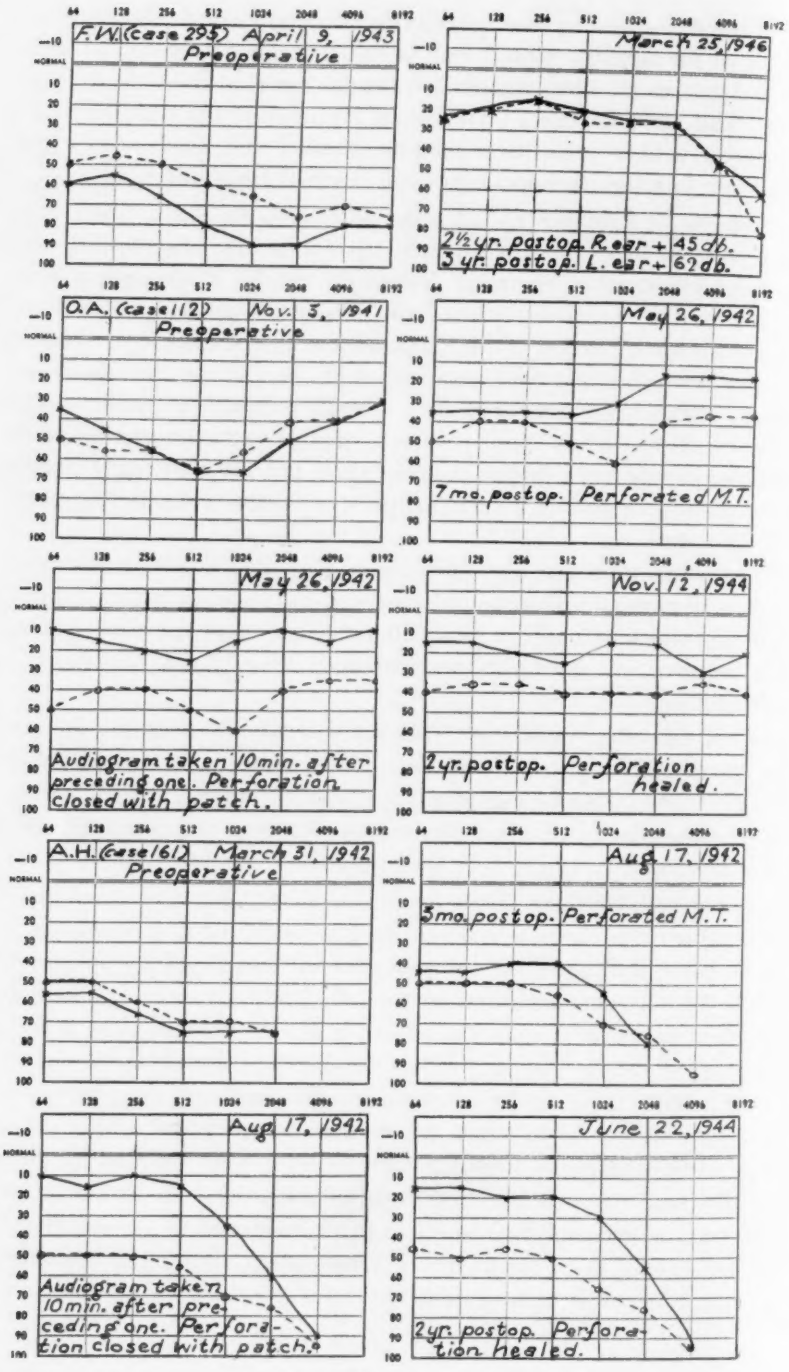
F.W. (Case 295) April 9, 1943
Preoperative
March 25, 1946
2½ yr. postop. R. ear + 45 db.
3 yr. postop. L. ear + 62 db.
O.A. (case 112) Nov. 3, 1941
Preoperative
May 26, 1942
7 mo. postop. Perforated M.T.
May 26, 1942
Audiogram taken 10 min. after preceding one. Perforation closed with patch.
Nov. 12, 1944
2 yr. postop. Perforation healed.
A.H. (case 161) March 31, 1942
Preoperative
Aug. 17, 1942
3 mo. postop. Perforated M.T.
Aug. 17, 1942
Audiogram taken 10 min. after preceding one. Perforation closed with patch.
June 22, 1944
2 yr. postop. Perforation healed.

Figure 6

(See legend on opposite page)

2. Placing the tympanomeatal skin flap under tension. By means of a small, plain gauze pack placed against the upper edge of the tympanomeatal skin flap above the fistula in the groove that has been hollowed out in skeletonizing the superior semicircular canal, the flap is placed under tension between the pars tensa of the tympanic membrane and the fistula. This tends to decrease the area over which the flap is attached to the bone between the fistula and the facial nerve, thus enhancing the sound vibrations transmitted to the fistula.

3. Preservation of the mucosa covering the bony horizontal semicircular canal. By rotating the dental finishing burr in such a direction as to lift up the mucosa of the middle ear on the surface of the bony horizontal semicircular canal toward the middle ear, this mucosa may be preserved close to the inferior edge of the fistula in many cases (fig. 2). This tends to decrease the area over which the flap is attached to the bone between the fistula and the facial nerve, enhancing the sound waves transmitted from the tympanic membrane to the fistula.

While it is difficult to prove statistically that these minutiae are important, the average gain of 30 decibels achieved since they were added to our technic may be significant.

Features to Lessen Postoperative Serous Labyrinthitis.—Postoperative serous labyrinthitis has loomed ever larger as the most frequent cause of failure in our experience as the causes for bony closure have been brought out and appropriate measures adopted. For a long time our efforts to lessen or to prevent postoperative serous labyrinthitis were without tangible results. Infection of the wound has been virtually eliminated by orthopedic preparation of the outer ear, by the use of ultraviolet Sterilamps in the operating room, by a meticulous aseptic operative and postoperative technic and by prophylactic chemotherapy.

EXPLANATION OF FIGURE 6

The small numbers at the top of each audiogram represent double vibrations per second (tonal frequencies); those at the left, decibels. Hearing for air-conducted tones is shown in the curves (right ear, circles; left ear, crosses).

Patient F. W. is represented by three audiograms, arranged from left to right; patients O. A. and A. H., by four audiograms each. The initials of the patient and the dates of the audiometric tests are given near the top in each set of audiograms.

The decibel gains stated below the curves are gains in the speech range.

An unusually great hearing improvement is shown in patient F. W., who also showed marked nystagmus when light pressure was applied to the lower edge of the tympanic membrane (the fistula test), indicating excellent mobility between the tympanic membrane and the fistula.

Patient O. A. experienced acute suppurative otitis media six months after operation, which cleared up but left a central perforation of the drum membrane 3 mm. in diameter.

Patient A. H. had a postoperative perforation of the tympanic membrane.

Experimental studies on the monkey have suggested that postoperative serous labyrinthitis is due more to the effect of blood and serum escaping from the skin flap into the perilymph space than to infection. Analysis of our clinical results has shown that excessive capillary bleeding during the operation was a frequent factor in the cases in which a further loss of hearing was experienced due to postoperative labyrinthitis. Most of the patients whose hearing was thus affected were men, whereas the majority of our fenestration operations are in women. Therefore we have instituted the procedure of removing 500 cc. of blood three days before operation in all men to stimulate the hemopoietic activity of the bone marrow. Again, it is difficult to prove statistically that this measure is beneficial, though the results thus far secured are encouraging.

Other measures to decrease bleeding during the operation have been those of administering Koagamin (a parenteral hemostatic containing oxalic and matonic acids) before and during the operation and elevating the head of the patient's bed 18 inches (46 cm.) for the first twelve hours after operation. After trying various anesthetics, including solution of tribromethanol U.S.P. sodium, intravenous pentothal and nitrous oxide, alone or in combination, we have returned to strictly local anesthesia as employed by Lempert, but with smaller doses of sedatives.

Despite all of these measures, postoperative serous labyrinthitis continued to be our most frequent cause of failure. The mobile cartilaginous stopple, used in 8 consecutive cases, did not prevent the usual postoperative drop in hearing due to serous labyrinthitis, and the hearing results were less favorable than in cases in which the stopple was not used. Therefore, we discontinued the use of the stopple, at least until published statistics on the two year results would be available, permitting evaluation of this technic.

Further experimental studies of the postoperative serous labyrinthitis of the monkey revealed the following significant facts:

Immediately after the fenestration operation the tympanomeatal skin flap covering the fistula shows a marked reaction consisting of capillary dilatation and increased capillary permeability, with red blood cells and serum escaping into the connective tissue of the flap and into the perilymph space at the fistula (fig. 5, upper part). This reaction is, we know, due to the histamine and histamine-like substances liberated from the traumatized soft tissues. By the fourth day the capillary dilatation begins to subside and the skin flap, thickened by the accumulation of red blood cells and serum, begins to return to normal. In the perilymph space at the fistula the delicate arachnoid mesh shows a slight to marked cellular reaction with fibroblasts, lymphocytes and macrophages (fig. 7). This reaction, which we may call acute proliferative arachnoiditis, serves to remove the red blood cells and serum that have accumulated. The

arachnoiditis may then resolve and resorb, or if it is severe, permanent fibrosis may remain in the perilymph space at the fistula, and some or all of the fibrous tissue may be replaced with new bone.

Meanwhile red blood cells and serum gravitate to the cochlea. In the cochlea, however, there is no arachnoid mesh in the perilymph spaces of the scala vestibuli and the scala tympani to remove the blood, and the red cells settle in the dependent portions of these ducts, where they may be found as long as a month after operation (fig. 5, lower part). The endolymphatic system remains free from red blood cells, but the sterile inflammatory reaction at the fistula and perhaps the presence of

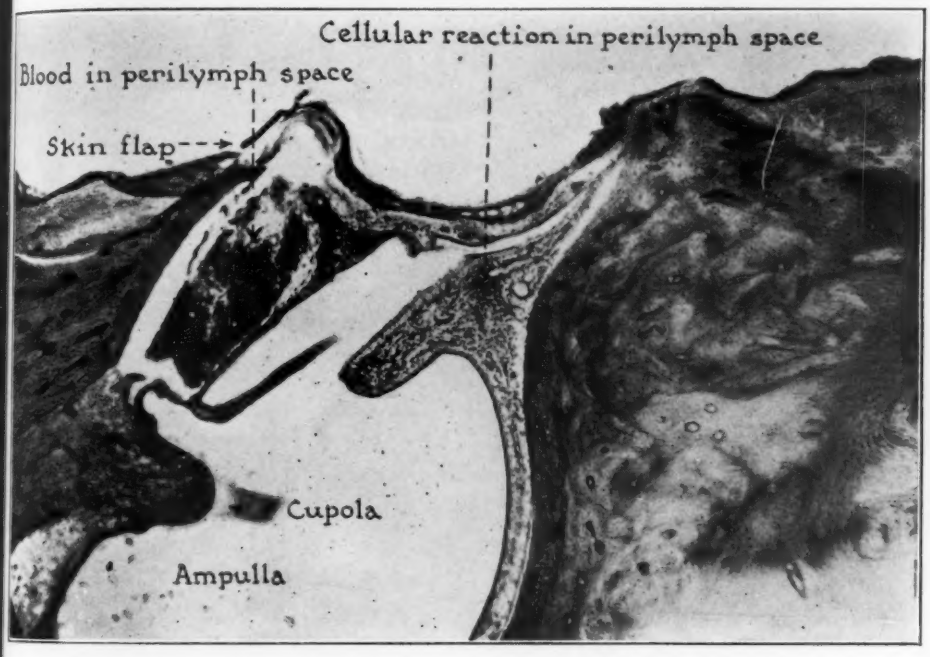

Fig. 7.—Fistula showing blood in the perilymphatic space of the labyrinth, with acute proliferative arachnoiditis four days after operation (monkey).

stagnant blood and serum against the very thin walls of the endolymphatic duct cause a serous or fibrinous exudate to accumulate in the ductus cochlearis (fig. 8). If this is slight, it may resorb without permanent damage to the organ of Corti, but if severe it leads to an "adhesive degeneration" of the organ of Corti, where Reissner's membrane, the tectorial membrane and the hair cells become glued together, with degeneration of hair cells (fig. 5, lower part).

Clinically the postoperative serous labyrinthitis is evidenced by postoperative spontaneous nystagmus, generally with the quick component

toward the ear not operated on, but sometimes there is "vascular nystagmus" with a rhythmic pendular to and fro movement synchronous with the pulse. The hearing is depressed, and the patient will frequently exhibit the symptom of binaural dysharmonic diplacusis.

The problem of the prevention of severe postoperative serous labyrinthitis narrowed down in our clinical and experimental studies to the problem of minimizing the inflammatory reaction of the skin flap, and to that of preventing the blood cells and serum from gravitating to the cochlea.

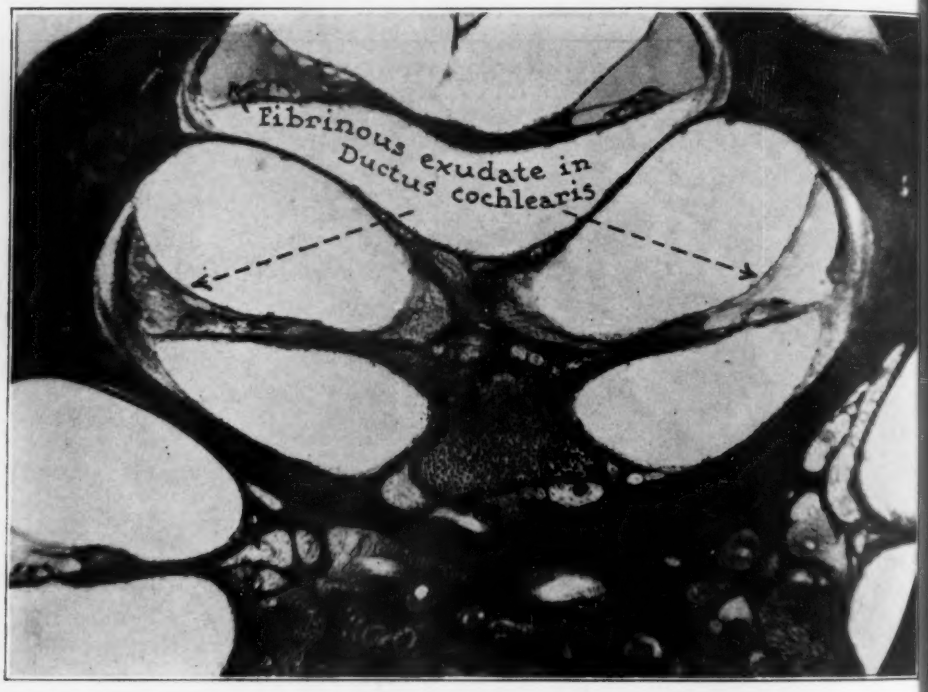

Fig. 8.—Cochlea showing fibrinous exudate filling the endolymphatic space one week after operation (monkey).

Two measures have recently been adopted which give promise of partially solving these two problems. These are the use of sea sponge packing and a head frame to maintain the cochlea in the treated ear in a position superior to, rather than dependent to, the fistula. While it is too early to judge the ultimate effect of using the sea sponge and head frame technic to minimize labyrinthitis, the early hearing results that have thus far been secured are striking and gratifying. Particularly noteworthy has been the frequent absence of the high tone drop which we were accustomed to expect during the first few weeks after operation

(fig. 9) and which in some cases disappeared many months later but in others remained as a permanent further loss for the tones of high pitch.

The rationale of the sea sponge technic of preventing labyrinthitis is as follows:

The capillary dilatation with increased capillary permeability in the skin flap that causes or contributes to postoperative serous labyrinthitis is due to histamine and histamine-like substances liberated in the skin flap by unavoilable operative trauma. The stagnation of the blood of the dilated capillaries tends to prolong and intensify the histamine effect, while the breaking down and absorption of the blood cells and serum that have escaped into the connective tissue of the flap further increase the accumulation of histamine. Waterproof paraffin or petrolatum packs tend to keep escaped serum and blood cells imprisoned in the cavity against the skin flap, contributing further to the local histamine effect.

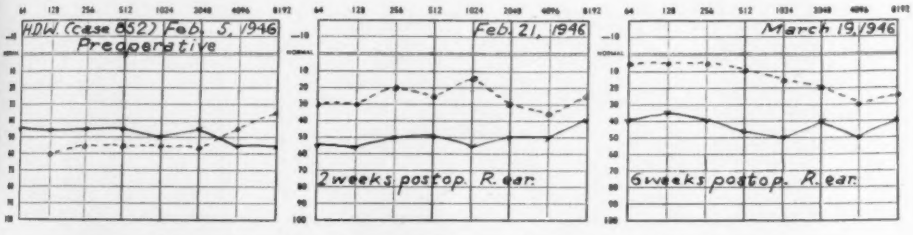

Fig. 9.—Audiograms of patient H. D. W. In the operation the sea sponge and head frame technic was used to decrease postoperative serous labyrinthitis. Note the early improvement in hearing for all frequencies, including those of high pitch.

Moreover, paraffin and petrolatum packs fail to provide the constant elastic pressure needed to keep the capillaries squeezed dry.

These principles have been known to general surgeons,[10] who have found that elastic absorbent sea sponge packs maintained with considerable pressure against skin grafts and large wounds result in a marked decrease in the postoperative devitalization of the margins of the skin and in the postoperative inflammatory edema of the skin.

Applying these principles to the fenestration operation we now place a single strip of plain gauze moistened in Ringer's solution against the tympanomeatal skin flap. To facilitate the subsequent painless removal of the sea sponge packs, either a paraffin gauze (Mosher) or a perforated rubber tissue basket, open at the bottom, is placed in the operative cavity. Pieces of sterilized sea sponge squeezed out of a suspension of sulfadiazine powder in Ringer's solution are inserted into the basket against the strip of plain gauze covering the flap (fig. 10). The cutaneous incision is sutured and another piece of sea sponge is inserted under considerable

10. Shambaugh, P.: Personal communication to the authors.

pressure beneath the sutured incision. A final large piece of sea sponge is placed over the external auditory meatus, and dry gauze dressings are applied, piled up over the ear to exert continuous pressure.

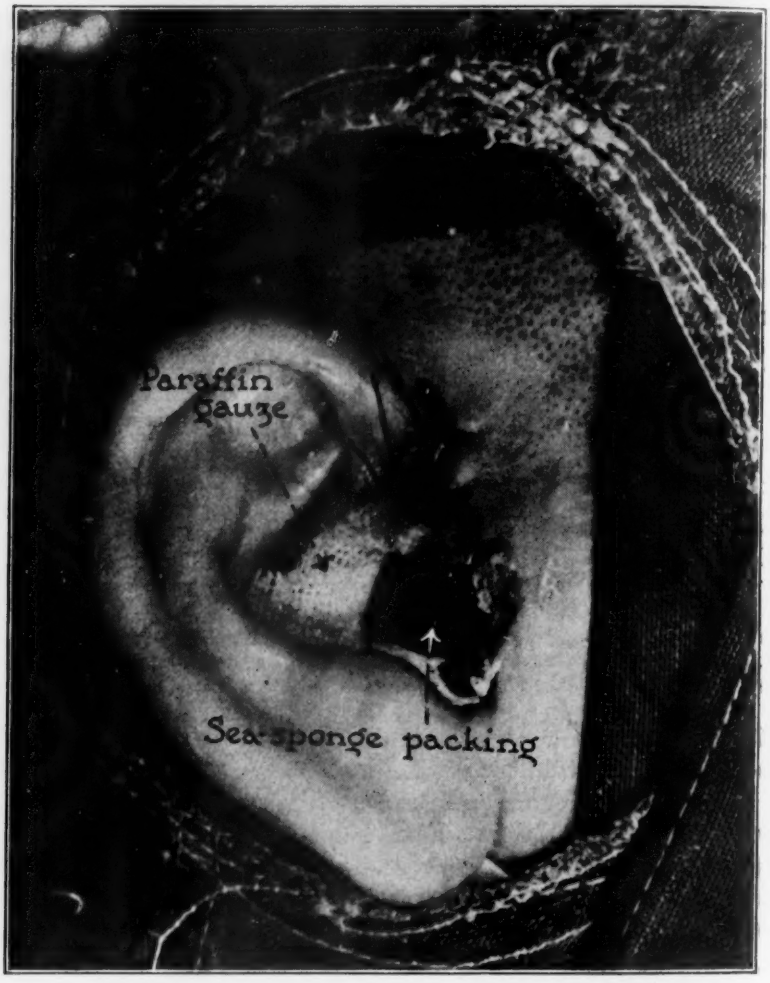

Fig. 10.—Sea sponge packing used after fenestration operation.

This initial dressing is not touched for six days. On the sixth day the sea sponge packs and paraffin basket are removed, the cavity is dusted with sulfadiazine powder, but the plain gauze strip lying immediately against the tympanomeatal skin flap is not disturbed until the tenth day. In this way the skin flap over the fistula remains immobilized for ten full days. On the tenth day, the last gauze strips are removed, and the cavity is painted with tincture of merthiolate.

1:1,000, and dusted with sulfadiazine powder. On the fourteenth postoperative day the cavity is painted with tincture of merthiolate and dusted with sulfadiazine powder. On the twenty-first, twenty-eighth and forty-second postoperative days the cavity is painted with 2 per cent aqueous solution of methylrosaniline chloride U.S.P. and thereafter not oftener than once a month until it is completely epidermized and healed.

The only deviation from this routine is made in the very rare case in which a purulent discharge develops; in that case the ear should be dressed every day or two until the infection has cleared.

The effect of this routine on the postoperative course has been to reduce the total number of postoperative dressings before the ear is completely epidermized and healed, to an average of about 6.

Especially surprising and striking has been the small amount of matter draining from the sea sponge packs onto the gauze dressings, also the dry character of the sea sponge packs and of the cavity when the packs are removed.

Equally striking and significant has been the absence of coagulated serum in the operative cavity at subsequent dressings after removal of the packs. Frequently we used to find the cavity almost filled with serum and fibrin two days after removing the waterproof paraffin or petrolatum packs. This change is evidence that the sea sponge technic is greatly lessening the increase of capillary permeability in the soft tissues.

The rationale of the head frame is this. We observed that blood cells and serum accumulated in the dependent portions of the cochlea in the monkey, owing to gravitation (fig. 5, lower part). After the fenestration operation the patient prefers to lie on the untreated ear; thus the cochlea of the treated ear is dependent to the fistula. By means of a simple head frame devised by Dr. Charles Whitaker, the resident otolaryngologist of the Wesley Memorial Hospital, the patient is kept lying only on his back or on the treated ear, so that the cochlea is superior to the fistula at all times (fig. 11). The patient is required to stay in bed for four days after the operation and then is allowed up. The result of this immobilization of the head has been to diminish greatly the degree and the duration of postoperative vertigo, nystagmus, vomiting and ataxia. With very few exceptions, our patients are now discharged from the hospital immediately after their first dressing on the sixth day following operation.

The hearing results thus far observed with the sea sponge and head frame technic afford proof of the lessened cochlear damage from serous labyrinthitis. A majority of patients now maintain a definite hearing improvement throughout the postoperative period (fig. 9),

whereas previously a considerable postoperative depression of hearing was observed in the majority, reaching its lowest level about one week after operation.

The ultimate value of the sea sponge and head frame technic to lessen labyrinthitis will not be known until two year hearing results are available in a consecutive series of 100 or more cases. It is logical to expect that the reduction in the postoperative labyrinthitis will not increase the frequency of bony closures, already reduced to

Fig. 11.—Head frame used to maintain the cochlea of the fenestrated ear in a position superior to the fistula.

less than 5 per cent after two years, and that the sea sponge and head frame technic therefore will result in a substantial increase in the proportion of permanent satisfactory hearing improvements.

SUMMARY

1. The two year hearing results of the fenestration operation may be considered the permanent hearing results.

2. Experimental studies of the fenestration operation in the monkey have brought out certain factors that influence the osteogenesis tending to close the fistula. The application of these factors to the human operation has reduced the incidence of the failure due to bony closure to less than 5 per cent in patients tested after two years.

3. The adoption of features to improve the mobility of the tympanomeatal skin flap between the tympanic membrane and the fistula has increased the average number of decibels gained from 28 to 30.

4. Postoperative serous labyrinthitis has been the most frequent cause of failure since the measures to prevent bony closures were adopted. The blood cells and serum that escape into the labyrinth from the skin flap appear to be the chief cause of this labyrinthitis. The sea sponge and head frame technic for preventing labyrinthitis has resulted in a striking improvement in the early hearing results and may be expected to improve the permanent hearing results.

5. The new fenestration technic developed at Northwestern University departs from other technics in a number of ways, the most important of which are:

(*a*) It assures enchondralization of the fistula.

(*b*) It includes constant irrigation of the operative field and use of the microscope while the fistula is being made.

(*c*) It scrupulously avoids traumatization of the endosteum within the labyrinth.

(*d*) It places the fistula on the horizontal semicircular canal laterally.

(*e*) It makes use of a sea sponge and head frame technic to prevent postoperative serous labyrinthitis.

LATE SECONDARY TONSILLAR HEMORRHAGE

II. Studies of Ascorbic Acid

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IT HAD been suspected for some time that vitamin C deficiency is an important biologic factor in impairment of wound healing. However, not until Lanman and Ingalls,[1] in 1937, demonstrated that scorbutic guinea pigs exhibited healing of operative incisions inferior to that of nonscorbutic controls did surgeons come to have a widespread interest in the role of ascorbic acid in tissue repair. The recent literature contains a great number of experimental and clinical observations substantiating a causal relationship between vitamin C deficiency and defective healing of wounds. It is not within the scope of this paper to review the work reported along these lines. The interested reader is referred to an article by Ruskin,[2] who discusses pertinent findings of various investigators.

It has become common in general surgical practice to administer vitamin C preoperatively and postoperatively in cases in which the level of ascorbic acid is below normal, thus safeguarding against defective reparatory processes. For instance, Whipple[3] stressed the effect of C-avitaminosis and C-hypovitaminosis in delaying wound healing. He cautioned that patients with a history of restricted diet should be regularly tested "for blood vitamin C content and not operated upon until the deficiency is corrected." Many other outstanding surgeons have expressed similar views.

From the Pharyngology Research Laboratory, Department of Otolaryngology, Columbia University College of Physicians and Surgeons, and Presbyterian Hospital, New York, and Hoffmann-La Roche, Inc., Nutley, N. J.

1. Lanman, T. H., and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing: Experimental and Clinical Study, Ann. Surg. **105**:616-625 (April) 1937.

2. Ruskin, S. L.: Vitamin C–Sulfonamide Compounds in the Healing of Wounds, Arch. Otolaryng. **40**:115-122 (Aug.) 1944.

3. Whipple, A. O.: The Critical Latent or Lag Period in the Healing of Wounds, Ann. Surg. **112**:481-488 (Oct.) 1940.

Surprisingly enough, otolaryngologists have paid little heed to the question of vitamin C adequacy in connection with their operations. This holds particularly with respect to tonsillar operations, which are not infrequently complicated by impaired healing of wounds, manifested by secondary hemorrhage. Myerson [4] alone has suggested that vitamin C deficiency is a factor in tonsillar bleeding and he recommended that "all patients should be given extra fruit juices for two or three days prior to the time of operation." However, he did not determine the vitamin C levels of his patients or correlate results in comparable groups of patients with and without administration of ascorbic acid.

PART I

By Harry Neivert and Recha Engelberg

In order to appraise objectively the significance of a state of vitamin C deficiency as an etiologic factor in late tonsillar hemorrhage, it was decided to study preoperative and postoperative blood plasma levels of ascorbic acid in a series of patients, to correlate findings with the episodes of bleeding and to evaluate the merits, if any, of ascorbic acid in decreasing the incidence of hemorrhage.

MATERIAL, PROCEDURE AND FINDINGS

The preoperative and postoperative plasma levels of vitamin C in 246 patients who underwent tonsillectomy were determined. In carrying out the estimations the method of Mindlin and Butler [5] was used. According to this technic, the decrease in the concentration of oxidized indophenol produced by the addition of an amount of plasma which is insufficient to cause complete reduction of the dye is measured by a photoelectric colorimeter.

According to Abt and Farmer,[6] vitamin C values below 0.7 mg. per hundred cubic centimeters of blood plasma are subnormal or suboptimal. Other investigators have placed the lower limits of normality at 0.6 mg. In this study 0.5 mg. was chosen arbitrarily as borderline, and all findings at this level or below were considered as reflecting a state of vitamin C deficiency and will be referred to as subnormal for the sake of convenience.

Among the 246 patients studied, the preoperative plasma level of vitamin C was above 0.5 mg. per hundred cubic centimeters in 112 and subnormal in 134. Reexamination of the patients on the fifth to the eighth postoperative day revealed that of the 112 with normal values preoperatively, 28 had subnormal values after tonsillectomy. Thus a total of 162 exhibited hypovitaminosis C either preoperatively or postoperatively.

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4. Myerson, M. C.: Hemorrhage Following Tonsillectomy, Am. J. Surg. **36**:151-158 (April) 1937.

5. Mindlin, R. L., and Butler, A. M.: The Determination of Ascorbic Acid in Plasma: Macromethod and Micromethod, J. Biol. Chem. **122**:673-686 (Feb.) 1938.

6. Abt, A. F., and Farmer, C. J.: Vitamin C: Pharmacology and Therapeutics, in The Vitamins: A Symposium, Chicago, American Medical Association, 1939, pp. 411-442.

There was a total of 21 late hemorrhages, and 15 of these occurred in the group with subnormal plasma levels of vitamin C preoperatively (not only a copious hemorrhage but the slightest escape of blood manifested by oozing or clot formation was counted as bleeding). Of the 6 hemorrhages in patients with normal preoperative ascorbic acid values, 4 occurred in those who postoperatively became deficient in vitamin C and 2 in those who showed normal values after tonsillectomy. Consequently, in the group of 162 patients whose values were subnormal either preoperatively or postoperatively, there were 19 hemorrhages. These observations are shown graphically in chart 1. Forty-nine of the 84 patients whose plasma levels of vitamin C remained above 0.5 mg. per hundred cubic centimeters showed a decrease in concentration of plasma ascorbic acid after tonsillectomy as compared with preoperative values.

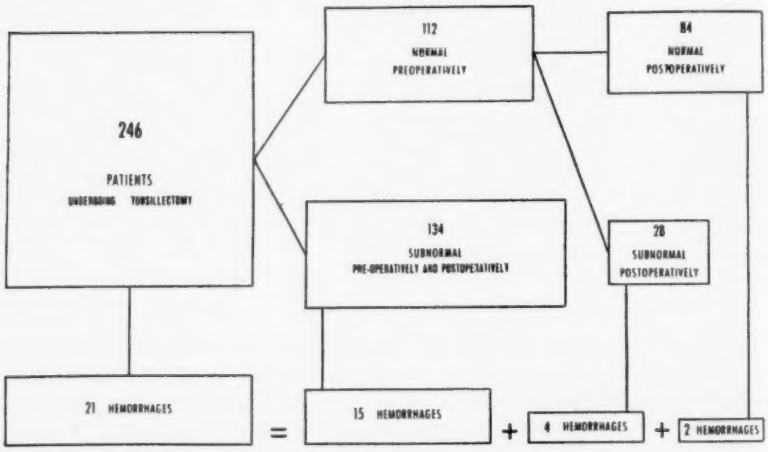

Chart 1.—Relation of postoperative hemorrhages to preoperative and postoperative blood plasma levels of ascorbic acid in 246 patients undergoing tonsillectomy. Five-tenths milligrams or less of ascorbic acid per hundred cubic centimeters of plasma is considered subnormal, more than 0.5 mg., normal. Nineteen of the total of 21 hemorrhages occurred in the group of 162 patients exhibiting hypovitaminosis C either before or after tonsillectomy. The areas signifying hemorrhages are not in proportion to the areas portraying vitamin C levels.

In a comparable series of 197 patients with tonsillar disease a daily dose of 300 mg. of vitamin C [7] was given for three to six days prior to tonsillectomy and for one week postoperatively. For many of these the vitamin C of the blood plasma was estimated after tonsillectomy, and in every instance the level was far above 0.5 mg. per hundred cubic centimeters. It is worthy of note that the general condition of the patients in this series was more satisfactory, that their tonsillar fossae looked much cleaner and that their wounds generally healed better than the wounds in the first series, in which the patients did not receive ascorbic acid.

Eight among these 197 patients were troubled by late tonsillar hemorrhage.

All patients of both series were permitted to use liberal amounts of acetylsalicylic acid for relief of pain on the days following tonsillectomy.

7. Hoffmann–LaRoche, Inc., Nutley, N. J., supplied Vitamin C 'Roche' Tablets for use in this study.

COMMENT

The foregoing data demonstrate that in a series of 246 patients the preoperative concentration of plasma ascorbic acid was below normal in 54.5 per cent and that, in addition, 11.3 per cent acquired a vitamin C deficiency after tonsillectomy.

Other investigators have reported somewhat similar observations. For instance, Holman [8] showed that 57 per cent of his ordinary "run of the mill" surgical patients were deficient in vitamin C, and Lund [9] demonstrated that some patients will show a fall of vitamin C levels following certain surgical operations. With respect to patients undergoing tonsillectomy, the operation may be responsible for the latter phenomenon, as well as acetylsalicylic acid, which has been shown to cause increased excretion of ascorbic acid.[10]

Furthermore, it will be noted from the data presented that in the control series of 246 patients the incidence of secondary tonsillar hemorrhage was 8.5 per cent and that proportionally many more bleeding episodes occurred among those patients whose concentration of plasma ascorbic acid was subnormal either preoperatively or postoperatively. On a percentage basis there were about five times as many hemorrhages among C-deficient patients as there were among those with normal postoperative levels of ascorbic acid. These findings constitute corroboratory evidence that C-hypovitaminosis delays wound healing, which in patients undergoing tonsillectomy may be manifested by a propensity to bleed.

In the series of 197 patients receiving vitamin C therapy the incidence of late hemorrhage was 4.1 per cent. As compared with that of 8.5 per cent which obtained in the series of patients who were not given ascorbic acid, this is a significant reduction.

PART II

By Leo A. Pirk and Recha Engelberg

Neivert [11] recently demonstrated that salicylate-induced hypoprothrombinemia is one of the most important factors in late tonsillar hemorrhage; that by using the water-soluble vitamin K-like compound

8. Holman, E.: Vitamin and Protein Factors in Preoperative and Postoperative Care of the Surgical Patient, Surg., Gynec. & Obst. **70**:261-269 (Feb. 15) 1940.

9. Lund, C. C.: The Effect of Surgical Operations on the Level of Cevitamic Acid in the Blood Plasma, New England J. Med. **221**:123-127 (July 27) 1939.

10. Daniels, A. L., and Everson, G. J.: Influence of Acetysalicylic Acid (Aspirin) on Urinary Excretion of Ascorbic Acid, Proc. Soc. Exper. Biol. & Med. **35**:20-24 (Oct.) 1936.

11. Neivert, H.: Late Secondary Tonsillar Hemorrhage: I. Studies of Prothrombin and Vitamin K, Arch. Otolaryng. **42**:14-18 (July) 1945.

Synkayvite (2-methyl-1,4-naphthohydroquinone diphosphoric acid ester tetrasodium salt) in conjunction with acetylsalicylic acid the prothrombinopenic effect of the latter was eliminated, and that the incidence of bleeding was thereby markedly reduced. How do these findings tie in with the observation that a low plasma content of vitamin C favors late tonsillar hemorrhage and that, on the other hand, saturation with ascorbic acid decreases the incidence of bleeding? If a large percentage of late tonsillar hemorrhages is due to the effect of salicylate on prothrombin, then, in the light of the present clinical results it seemed likely that vitamin C also would afford protection against salicylate-induced hypoprothrombinemia. It therefore became desirable to determine whether ascorbic acid actually had such an effect.

EXPERIMENTS

Five normal subjects (1 man, 4 women) ranging in age from 24 to 65 were chosen. Their nutritional state was satisfactory, and they were requested to maintain well balanced and constant diets throughout the experimental period.

Studies of Prothrombin Time.—In carrying out estimations of prothrombin time the Page[12] method was used. According to this technic, viper venom and calcium chloride are added to plasma obtained by centrifuging decalcified venous blood. The sharp end point is characterized by the formation of fibrin particles clearly visible in the agitated test tube. For each person, estimations of prothrombin time were performed on three consecutive days. The control values thus obtained for the individual subjects were in close agreement. In 4 the prothrombin time was normal; in 1 it was longer than normally encountered.

The experiments which follow may be divided into four phases.

First Experimental Phase: Each person received 40 grains (2.6 Gm.) of acetylsalicylic acid a day divided into four doses (occasionally, if a subject neglected to take a dose, the daily total was 30 grains [1.9 Gm.] only). In all cases salicylate-induced prothrombinopenia became evident after two to six days, but the taking of acetylsalicylic acid was continued until the total intake amounted to 290, 320, 330, 380 and 420 grains (18.5, 20.4, 21, 24.3, 26.9 Gm.) respectively. The corresponding prolongations of prothrombin time at the end of these courses were 5.3, 6.7, 13.8, 3.7 and 4.8 seconds. The spectacular rise of 13.8 seconds occurred in the subject whose premedication control had shown impaired prothrombin activity.

Second Experimental Phase: A few days after discontinuance of the taking of acetylsalicylic acid the raised prothrombin times returned to their original values. Subsequently, each of the subjects was placed on the combined medication of 40 grains (2.6 Gm.) of acetylsalicylic acid and 400 mg. of ascorbic acid daily, both divided into four doses. This dosage was continued at least over a period equivalent to that in which acetylsalicylic acid alone had been administered. Determinations of prothrombin time carried out at frequent intervals showed that the concurrent intake of vitamin C afforded full protection against salicylate-induced prothrombinopenia in all 5 persons.

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12. Page, R. C.; de Beer, E. J., and Orr, M. L.: Prothrombin Studies Using Russell Viper Venom: Relation of Clotting Time to Prothrombin Concentration in Human Plasma, J. Lab. & Clin. Med. **27**:197-201 (Nov.) 1941.

Third Experimental Phase: At this point ascorbic acid was withdrawn and the subjects thus received again a daily dose of 40 grains of acetylsalicylic acid alone until the total intakes amounted to 290, 400, 600, 600, and 380 grains (18.5, 25.6 38.4, 38.4, 24.3 Gm.) respectively. Again, in every case a significant prolongation of the prothrombin time was observed.

Fourth Experimental Phase: Several days after discontinuation of the intake of acetylsalicylic acid the raised prothrombin times regressed to premedication values. Subsequently the effect on the prothrombin levels of another course of combined administration of acetylsalicylic acid and vitamin C was studied. As during the second experimental phase, a daily total dose of 40 grains (2.6 Gm.) of acetylsalicylic acid and of 400 mg. of ascorbic acid was given to each person. The period of administration ranged from seven to fifteen days. Repeated determinations of prothrombin time corroborated the findings of the previous corresponding experiments, namely, that the concurrent intake of vitamin C affords protection against salicylate-induced prothrombinopenia. There was just one reading (subject E. N., chart 2, sixty-first day of observation) which reflected lowered prothrombin activity in spite of the intake of ascorbic acid. However, the subject at that time was suffering from a severe cold, a condition which has been found to have a hypoprothrombinemic effect in trials not pertaining to this work. When the cold subsided, the prothrombin time returned to normal.

Studies of Ascorbic Acid Content of Blood Plasma and of Thrombocyte Level.—In addition to the determinations indicated in the foregoing section, repeated determinations of the plasma vitamin C and platelet levels of all 5 persons were made.

Representative Effects of Acetylsalicylic Acid and of This Acid in Conjunction with Ascorbic Acid on the Prothrombin Time, the Blood Plasma Concentration of Vitamin C and the Number of Thrombocytes of J. J. O'F., a White Man Aged 45; Protective Action of Ascorbic Acid Against Hypoprothrombinemia and Relative Thrombocytopenia, Both Induced by Salicylate Medication

	Total Doses	Days of Medication	Prothrombin Time, Seconds	Plasma Vitamin C, Mg. per 100 Cc.	Thrombocytes
Premedication findings.....	.....	..	20.7	0.45	256,000
Findings during:					
First experimental phase..	290 grains (18.5 Gm.) acetylsalicylic acid	7	26	0.33	192,000
Second experimental phase	280 grains (17.9 Gm.) acetylsalicylic acid + 2,800 mg. C.	7	20	1.41	256,000
Third experimental phase.	290 grains (18.5 Gm.) acetylsalicylic acid	7	25.6	1.00	216,000
Fourth experimental phase	280 grains (17.9 Gm.) acetylsalicylic acid + 2,800 mg. C.	7	21.5	1.00	244,000

A computation of findings in one of the subjects is given in the accompanying table. As will be noted, the premedication plasma concentration of vitamin C was 0.45 mg. per hundred cubic centimeters and the thrombocyte count 256,000 per cubic millimeter. Medication with acetylsalicylic acid (first experimental phase) resulted in a decrease in the plasma content of ascorbic acid to 0.33 mg. per hundred cubic centimeters and in the number of blood platelets to 192,000

per cubic millimeter. These changes were concomitant with lowered prothrombin activity as reflected in prolongation of the prothrombin time. Administration of vitamin C along with the acetylsalicylic acid (second experimental phase) resulted in a rise of the plasma content of ascorbic acid to 1.41 mg. per hundred cubic centimeters and of the number of blood platelets to 256,000 per cubic millimeter. Concurrently, the prothrombin time returned to its premedication value. Withdrawal of vitamin C and continuation of the use of acetylsalicylic acid (third experimental phase) reduced somewhat the plasma concentration of ascorbic acid and the number of thrombocytes. Simultaneously, the prothrombin level was deficient. Renewed medication with acetylsalicylic and ascorbic acid combined (fourth experimental

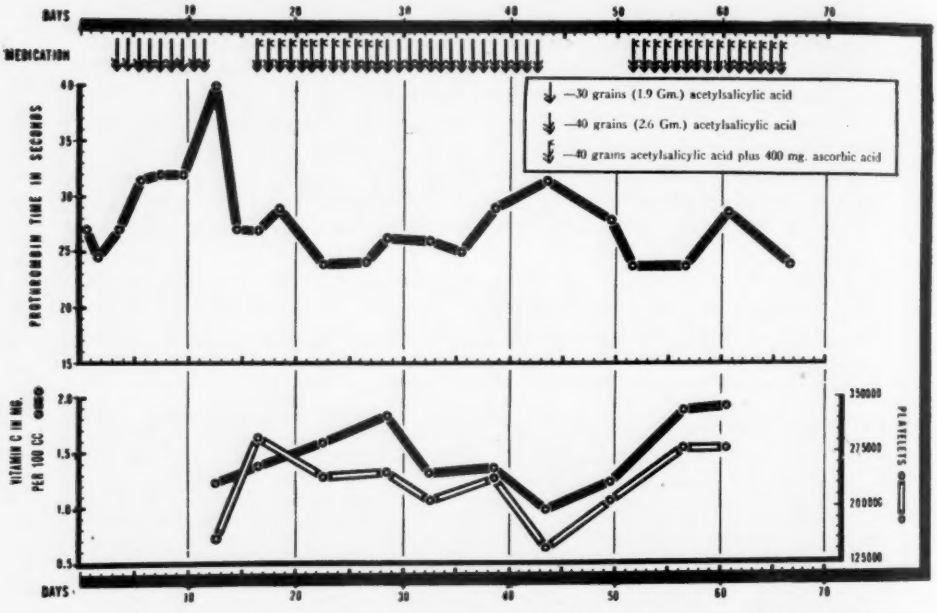
DAYS
MEDICATION
PROTHROMBIN TIME IN SECONDS
—30 grains (1.9 Gm.) acetylsalicylic acid
—40 grains (2.6 Gm.) acetylsalicylic acid
—40 grains acetylsalicylic acid plus 400 mg. ascorbic acid
VITAMIN C IN MG. PER 100 CC.
PLATELETS

Chart. 2.—Representative effects of acetylsalicylic acid on prothrombin time and the protective action of vitamin C in E. N., a white woman aged 34. In this chart and chart 3 it is shown that acetylsalicylic acid produces prolongation of the prothrombin time; that concurrent administration of ascorbic acid counteracts salicylate-induced prothrombinopenia; that continuation of the intake of acetylsalicylic acid without vitamin C causes another rise of prothrombin time; that renewed addition of vitamin C to the salicylate renders the prothrombinopenic influence of the latter ineffectual. In general, the number of thrombocytes is reduced and the blood plasma concentration of vitamin C is low when prothrombin activity is impaired.

phase) raised the thrombocyte concentration while the prothrombin time was at the premedication value.

Corresponding observations on 2 other subjects are presented in charts 2 and 3.

Evaluations of Findings.—In correlating the respective findings in the 5 subjects, it became evident that the prothrombinopenic action of acetylsalicylic acid is associated in general with a reduction of both plasma ascorbic acid and blood platelets; that, furthermore, 100 mg. of vitamin C administered in conjunc-

tion with each 10 grains (0.66 Gm.) of acetylsalicylic acid affords protection not only against salicylate-induced prothrombinopenia but also against reduction of thrombocytes and of plasma vitamin C.

COMMENT

In his studies on the effect of vitamin K on prothrombinopenia, Shapiro [13] found in a case of acute rheumatic endocarditis that a daily dose of 2 to 9 mg. of menadione failed to counteract the hypoprothrombinemia induced by a daily dose of 5 Gm. of acetylsalicylic acid. The administration of 400 mg. of vitamin C, by daily intravenous injec-

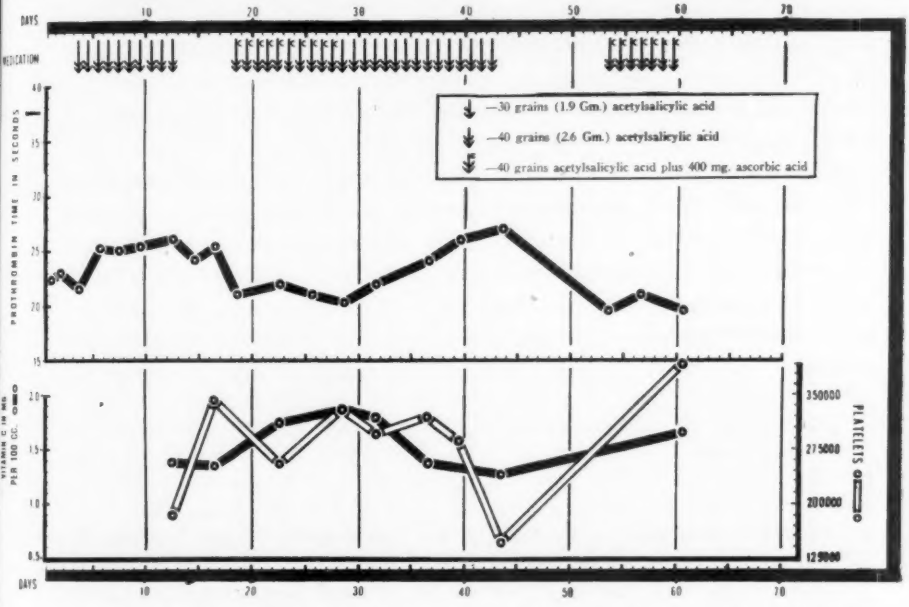

Chart 3.—Representative effects of acetylsalicylic acid on prothrombin time and the protective action of vitamin C in D. W., a white woman aged 24.

tion, on four consecutive days (in addition to the salicylate and the menadione) restored the prothrombin time to normal.

The present investigations furnish evidence that under the conditions of experimentation the administration of ascorbic acid by mouth without concurrent vitamin K medication affords protection against salicylate-induced prothrombinopenia.

The effect of ascorbic acid on the duration and the extent of the hypoprothrombinemia caused by dicumarol (3,3′-methylenebis

13. Shapiro, S.: Studies on Prothrombin: VI. The Effect of Synthetic Vitamin K on the Prothrombinopenia Induced by Salicylate in Man, J. A. M. A. **125**:546-548 (June 24) 1944.

[4-hydroxycoumarin]) was studied by Link and his associates.[14] These investigators found that in vitamin C–depleted guinea pigs the capacity to restore normal prothrombin levels after the administration of the anticoagulant is markedly impaired; that, furthermore, in the presence of abundant vitamin C there is decreased susceptibility to the hemorrhagic agent. Similarly, in the experiments presented, large doses of ascorbic acid protected the subjects from the prothrombinopenic effect of acetylsalicylic acid.

Vitamin C is thought to exert this protective action by virtue of its general detoxifying effect—a property observed by many workers. For instance, Pelner[15] demonstrated that salicylate toxicity (marked tinnitus) in a case of rheumatic fever was overcome by administration of ascorbic acid. The same investigator[16] and others showed that the toxicity of the sulfonamide compounds could be reduced by simultaneous intake of vitamin C. There also is evidence that arsenical sensitivity can be overcome by administration of ascorbic acid. Vail,[17] for instance, observed relief from symptoms of sensitivity to arsenicals when vitamin C was used along with arsenical drugs. Wuellner[18] holds that the toxicity of quinine is reduced when ascorbic acid is given in conjunction with the antimalarial drug. It is noteworthy that these drugs—sulfonamide compounds, arsenicals, quinine—cause hypoprothrombinemia. Therefore, it is suspected that vitamin C will counteract the

14. Overman, R. S.; Stahmann, M. A., and Link, K. P.: Studies on the Hemorrhagic Sweet Clover Disease: VIII. The Effect of 2-Methyl-1,4-Naphthoquinone and *l*-Ascorbic Acid upon the Action of 3,3′-Methylenebis (4-Hydroxycoumarin) on the Prothrombin Time of Rabbits, J. Biol. Chem. **145**:155-162 (Sept.) 1942. Baumann, C. A.; Field, J. B.; Overman, R. S., and Link, K. P.: Studies on the Hemorrhagic Sweet Clover Disease: X. Induced Vitamin C Excretion in the Rat and Its Effect on the Hypoprothrombinemia Caused by 3,3′-Methylenebis (4-Hydroxycoumarin), ibid. **146**:7-14 (Nov.) 1942. Sullivan, W. R.; Gangstad, E. O., and Link, K. P.: Studies on the Hemorrhagic Sweet Clover Disease: XII. The Effect of *l*-Ascorbic Acid on the Hypoprothrombinemia Induced by 3,3′-Methylenebis (4-Hydroxycoumarin) in the Guinea Pig, ibid. **151**:477-485 (Dec.) 1943.

15. Pelner, L.: The Effect of Ascorbic Acid (Vitamin C) on the Sensitivity to Salicylates in a Case of Rheumatic Fever, J. Lab. & Clin. Med. **28**:28-30 (Oct.) 1942.

16. Pelner, L.: Sensitivity to Sulfonamide Compounds Probably Avoided by Combined Use with Ascorbic Acid, New York State J. Med. **43**:1874 (Oct. 1) 1943.

17. Vail, A. D.: Influence of Vitamin C Therapy on Arsenical Sensitivity, J. Missouri M. A. **38**:110-120 (April) 1941.

18. Wuellner, W.: Tierexperimentelle Untersuchungen über die Einwirkung von Chinin, Redoxon und Chinin-Redoxon auf die Blutbakterizidie und Diurese, München. med. Wchnschr. **85**:785-786 (May 27) 1938.

mechanism by which these agents interfere with the production of prothrombin in much the same way as it does salicylate-induced or dicumarol-induced prothrombinopenia.

SUMMARY OF PARTS I AND II

Two comparable series of patients undergoing tonsillectomy were studied. The plasma levels of vitamin C of the control series were determined before and after operation. The preoperative concentration of ascorbic acid was subnormal in more than half of the patients and there was a decrease in the vitamin C content postoperatively in the majority of those whose original values had been normal. Most of the hemorrhages occurred in the patients with vitamin C deficiency. The patients of the second series were saturated with ascorbic acid, and in these the incidence of hemorrhage was significantly reduced.

The patients of both series received liberal amounts of acetylsalicylic acid. Since hypoprothrombinemia caused by salicylate has been shown to be one of the most important etiologic factors of secondary tonsillar bleeding, the beneficial results observed with ascorbic acid were thought to be indicative of a protective effect exerted by this vitamin against drug-induced prothrombinopenia. Experiments carried out in this direction bore out this suspicion. Evidence is presented that vitamin C prevents salicylate–induced hypoprothrombinemia. This effect is believed to be due to the detoxifying action of ascorbic acid.

In a subsequent report the results attending the combined administration of vitamins C and K will be presented.

NOTE.—Since submitting this article for publication, another report pertaining to the problem presented has been found. R. G. Macbeth (In Discussion on Influence of Vitamins and Hormones on Physiology and Pathology of Ear, Nose and Throat, *Proc. Roy. Soc. Med.* **36:** 625 [June] 1943) reported the absence of late tonsillar hemorrhage in patients who had been given ascorbic acid preoperatively. However, his series (13 patients in the group receiving vitamin C and 13 in the control group) is too small to warrant any definite conclusions.

Miss Ethel Nord, head nurse, collaborated in this study.

TREATMENT OF TUBERCULOSIS OF THE LARYNX

An Evaluation

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PULMONARY tuberculosis, as well as its more common complications, has been recognized for many centuries. These have passed under a variety of names, but the gross signs and symptoms representing them created a clinical picture which was apparently rather definite several hundred years before the Christian era. The clarification of the concept of tuberculosis has probably involved more space in the literature than that of any other disease. The recognition of the disease, now highly developed, is general; the proper treatment is somewhat less recognized or comprehended.

Tuberculosis, primarily a member of the chronic infectious granuloma grouping, is characterized by its protean complications. In its primitive state it is a relatively innocent disease. Its diffuse and troublesome manifestations have placed it at the top of the list as humanity's most persistent and prevalent disease. Among the various complications of this disease none has received more universal attention than the complication laryngeal tuberculosis. In spite of this fact, a review of its incidence as represented in the literature reveals a striking spread in percentages. Some of the prevailing disparity may be attributed to the fact that the tabulations are from different localities and different patient groupings. Some is apparently due to errors of diagnosis. Whether the percentages be large or small, laryngeal involvement is an ever present problem and its occurrence is attended usually by some alteration of the prognosis. Since it usually occurs among those with advanced pulmonary disease, the added burden to the patient, even though small, is of more than casual importance. During the past decade this complication has come to be regarded, however, in a somewhat softer light, and I feel that this general trend is of more significance than is immediately apparent. It is not that the treatment of laryngeal tuberculosis has differed or improved to any great extent, but rather that therapy of the primary pulmonary disease has so greatly advanced that its impact has been strongly felt in the realm of this formerly serious and significant complication.

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A casual review of the literature reveals a wide and certainly varied range of treatment. Many reports of therapeutic measures and results are obviously delete but should certainly be regarded as sincere, though inadequate, steps leading in the general direction of modern concepts. Some of the agents formerly employed have been cast aside in the general and special fields of therapy as being of no general or special value. The recent experimental studies of several members of the sulfonamide group of drugs have been somewhat encouraging, but suffice it to say that there has been no chemical agent which has been proved to have any direct demonstrable effect on the tubercle bacillus whether applied locally or administered orally. The newer antiseptic and bactericidal agents have not proved themselves of any value whatsoever in the treatment of laryngeal tuberculosis; this may be due in some slight degree to the inaccessibility of the laryngeal tissues and to the inability to reach the underlying pathologic process frequently enough to be of any practical benefit. The advent of more adequate collapse therapy has been somewhat misleading in that it has obscured the real and apparent effect of the various methods of treatment of laryngeal tuberculosis.

The correlation between the resolution of pulmonary and that of laryngeal tuberculosis has become more and more apparent in recent years, owing to more accurate methods of diagnosis and appraisal. With the advent of tomography and the more general use of lung mapping with radiopaque oil, there are today an appreciable number of cases in which diagnosis and prognosis have been altered as far as the pulmonary condition is concerned, and this alteration may be reflected on the laryngeal status, should this organ be involved. By the use only of a simple roentgenogram of the chest, a number of patients with laryngeal tuberculosis have been placed in a rather dire category.

Laryngeal tuberculosis apparently acquired its severe reputation of former years from the fact that the severe pulmonary tuberculosis which it usually accompanies was in a rather hopeless catagory itself. Since laryngeal tuberculosis is sometimes more prominent than the pulmonary condition in those patients who have both, the former was apparently deemed the more profound in the calculations of mortality. Today its presence, even in an advanced form, is not such a dire circumstance if the pulmonary disease can be held relatively in check.

The general and local effect of advanced pulmonary tuberculosis in an established case is usually of such a nature that it places the patient in an irrevocable category for the remainder of his natural life. This is not necessarily true of a severe laryngeal involvement if the pulmonary condition is of a mild character. The many factors involved in anticipating the future of tuberculous patients are sometimes vague and so

preclude the possibility of accurate forecasts in all except a few cases. The most accurate criterion for prognosis would seem to consist of permitting the patients to subsist on simple rest alone as a therapeutic test and subjecting them to periodic examinations to determine their somatic responses. That this is somewhat precarious is obvious to those acquainted with modern concepts of pulmonary therapy. In regard to the larynx, however, I feel that there is considerable justification for so doing inasmuch as pulmonary control is so often a method of choice in clearing the tuberculosis of the larynx. In tuberculosis, as in other fields of medicine, plans of therapy seem to follow cycles from passive stages to apparent overtreatment. This seems to be well borne out in the literature in many cases of laryngeal tuberculosis, and many laryngologists who are familiar with the subject have witnessed the end results of overenthusiastic laryngeal therapy.

In general, the prognosis of laryngeal tuberculosis is somewhat better than that of parenchymal involvement, as laryngeal resolution in the presence of pulmonary regression has been recorded in many cases. This seemingly paradoxic response is not easily accounted for. The two types of tissue involved may be the answer; more adequate drainage of the involved structures would seem to be a pertinent factor also. The fact that the larynx in the majority of cases of infection and neoplastic involvement holds its disease rather tenaciously within its confines, except when the process is terminal, may contribute in some fashion to the final answer also.

The phthisiologist is in a somewhat unfortunate position in that he treats a disease which he is never able to see; this fact does not hold true in the case of the laryngologist. Since the lung and the larynx are so closely associated if involved by tuberculosis, the laryngologist should be in an advantageous position to render aid in diagnosis and to a lesser degree in prognosis. It is sometimes the laryngeal disease which points a diagnostic finger in the direction of the pulmonary infection, but nevertheless there are numerous cases in which the upper passages have been assaulted operatively and otherwise, with total disregard of this axiomatic fact. The diagnosis of laryngeal tuberculosis is not as facile as many authors would lead one to believe, and I am of the impression that some of the reports in the higher percentages are in error. The accepted criteria for diagnosis include hoarseness. Only a very small percentage of patients in this sanatorium who attend our clinic complaining of this symptom have the complication of laryngeal tuberculosis; other factors such as laryngeal edema, simple irritation, local myasthenia and compromise of the recurrent nerve are predominant backgrounds for their hoarseness. The most accurate method of diagnosis would be by biopsy. This method, which usually involves a certain amount of destruction of normal tissues, unfortunately

infringes too greatly on physiologic principles to be of practical value. The danger of spread also precludes its use. Laryngeal tuberculosis is usually of a chronic nature and, except terminally, does not change rapidly one way or another. The patient with a diagnosis of laryngeal tuberculosis whose complication clears in a matter of days need not feel elated with good fortune; he probably did not have it in the first place. Some of these patients who have been treated by the various methods available have in the past probably been considered as having responded to whatever method or methods were employed on them. The addition of these seemingly remarkable results to the favorable register has not contributed at all to the therapeutic armamentarium. It would seem that appearance and chronicity are the two best criteria for the diagnosis of laryngeal tuberculosis. A fact which does not appear to have been stressed sufficiently is that the largest percentage of patients who contract tuberculosis have the symptom of persistent and rather intractable hoarseness which they think is a companion to their self diagnosed cold or "flu." This almost always clears up in a matter of days after the sanatorium regimen has been instituted and is usually forgotten by the patient, since subjective and objective attention is focused largely on the pulmonary tuberculosis. Many patients of this type have had the diagnosis of laryngeal tuberculosis insinuated on them erroneously.

An evaluation of therapeutic measures directed toward disease for which specific factors are available entails for the most part a problem of mathematics. Computations for indirect or nonspecific measures are always more intangible and incorporate personal opinion as an unavoidable factor. One contribution may enthusiastically champion a method or methods the results of which cannot be substantiated and which soon fall into the dim category of the empiric. It is far easier to evaluate the course of a disease if no specific treatment is used.

TREATMENT

The use of menthol in oil some years ago seemed to be the most popular form of therapy in laryngeal tuberculosis, and enjoyed wide acclaim, as did that of chaulmoogra oil. The glowing reports on the use of these substances apparently did not take into consideration the fact that tuberculosis is a self-healing disease if it heals at all. The placing of a heavy oil on the surface of a lesion which is already covered by a heavy protective coating does not seem to be therapeutically sound. This is all the more obvious since the exudate cannot be removed sufficiently or frequently enough, even if the oil-laden substance were able to accomplish beneficial results. These oils have some palliative features which may to some extent exonerate one who uses them. In a sense, a patient may feel somewhat improved

mentally if he feels something is being done for him; the value of menthol and associated volatile oils in the general field of medicine in all probability is limited in this respect. The familiar aroma of the volatile oils in medicaments is a nostalgic reminder of the days when patients had more done to them than for them.

Chemical cautery with silver nitrate, lactic acid and other similar substances has long held a legitimate therapeutic spot in the general field of medicine. These substances have been used extensively in the treatment of laryngeal tuberculosis and with a certain amount of reason. Their use, however, has been rendered rather impracticable by the inaccessibility of the basal pathologic changes. The local hyperemia induced by these irritants contributes to a modest degree to whatever resolution exists or to that which follows their use. The shallow ulcerations of the mucous membrane which are not infrequently encountered in the larynx can probably be totally extirpated in selected cases by this method. Once the lesion has broken through the basal membrane and into the underlying tissues, the use of cautery is certainly limited and the benefit dubious. The limitation of chemical cautery should be understood to the extent that it receives credit only for what it actually is able to accomplish. Since tuberculosis is characterized by a relatively poor general response, as well as unsatisfactory local reaction, any therapeutic measure which has a general or local stimulating effect should be seriously considered.

Ultraviolet ray therapy has long enjoyed extensive popularity in the general field of tuberculosis. In an earlier day it was considered as absolutely essential, regardless of the type of disease which was present. Before present day concepts of tuberculosis therapy were established, sunlight and a nutritious diet shared the only therapeutic halo available. Modern therapeutic measures have somewhat dimmed the luster of these two factors. Actually, certain types of pulmonary tuberculosis are probably rendered worse by irradiation. The use of ultraviolet rays is contraindicated in the acute exudative type of pulmonary or laryngeal tuberculosis. The use of ultraviolet rays, either natural or artificial, has until recently been widely accepted as a somewhat exalted therapeutic measure in laryngeal tuberculosis, and the various contrivances which were used to pipe the rays to the seat of the trouble were ingenious, though there probably was little benefit derived therefrom. It is doubtful whether under the very best of conditions more than a small fraction of the rays ever survived the trip through the various contours of the hypopharynx. Since ultraviolet rays are capable of penetrating only to a depth of a few millimeters, those which did reach their destination left the actual seat of trouble largely undisturbed. Generalized exposure to ultraviolet rays has come to be accepted by many as being most beneficial in extrapulmonary tuberculosis, and I

assume that laryngeal tuberculosis probably received some tangible aid from its use. It should be regarded solely as a supportive measure and nothing more.

In the past all known infections have at some time or another been subjected to high voltage roentgen ray therapy, and tuberculosis of the larynx is no exception. Here again the reports on its use range from unequivocal claims of success to casual refutation of such claims. Those who maintain a modest position on the subject describe benefits from the stimulating properties of its employment. That it should be beneficial in certain other infections is in no way disputed, nor should it be in this one if the indications are sharply defined. Its use is contraindicated in pulmonary tuberculosis. In the larynx its use should be limited to the productive and dry types of disease; if the disease is of the acute exudative variety, this therapy should be excluded. The exact manner in which it works, if it does, is not well comprehended, but whatever beneficial result ensues following its use is probably due to an incitement of tissue responses and not to a direct bacteriostatic or bactericidal phenomenon. As long as its limitations are recognized, its employment is certainly justified in laryngeal tuberculosis.

Far out in front in the modern methods of attack on laryngeal tuberculosis is electrocautery. After this method was developed and recognized it superseded all others for a decade or more. At the zenith of its popularity it was considered to be appropriate for all forms of laryngeal tuberculosis until more modern concepts of pulmonary therapy were developed. It has been recognized for some time that most infections in the body will do much better after an operative procedure if it is feasible to permit the body to wall off the infection to the greatest extent which good judgment will allow. If the body is not able to produce such a response, then cautery will be of no avail. If cautery is instituted before this has taken place, its employment may be expected to be disappointing not only from the standpoint of eradication of the disease but also from that of physiologic function. A considerable number of patients are to be seen today whose general physical condition is functionally far superior to their laryngeal status, and this I believe to be the result in the vast majority of instances of inopportune or overenthusiastic cauterization or both. An isolated lesion in the larynx may be totally and rapidly extirpated even though the pathologic process is deep seated. Inasmuch as the physiologic penalty is rather high in such a therapeutic maneuver, its employment should be reserved for only a few selected cases or for none at all. Electrocautery may be said to have two main functions. The first is the destruction of diseased tissues and the second a local stimulation of tissues due to the resultant hyperemia. Just what part

each plays in a given case cannot be determined with any degree of accuracy.

The role of general and local rest in tuberculosis, either primary or secondary, is one which cannot be overestimated. The part which general rest has played in this disease is the foundation of modern therapy in tuberculosis. Placing a local portion of the body at rest is, of course, the intention of collapse methods, and the application of this principle to an infected larynx is of no less importance. Many of the movements of the larynx cannot be controlled, but the most important one, that of talking, can easily be. It has been my impression for some time that placing the vocal cords at rest is by far the most important factor in the therapy of laryngeal tuberculosis, and I am presenting a small but representative series of unselected cases which emphasize the major role which it can play. I wish to point out that it is important only when coupled with adequate pulmonary control and that the two together are capable of rendering therapeutic dividends. It will be noticed that under rest alone the larynx is capable of resolution even in the presence of pulmonary regression. This sanatorium contains all the various types of cases except those in which a major surgical intervention is scheduled and those in which such intervention has recently been carried out.

Case 1.—S. T., a Negro aged 29, had a diagnosis of far advanced pulmonary and bronchial tuberculosis. The onset was in October 1942. The sputum was positive; the vital capacity, 71 per cent; the Kahn test, positive. Laryngeal tuberculosis was diagnosed on Nov. 19, 1942, ulcerative. The laryngeal lesion was resolving on December 31. The patient died on Jan. 21, 1943, with a pulmonary spread, probably due to the bronchial disease.

Case 2.—J. B., a Negro aged 47, had a diagnosis of minimal pulmonary tuberculosis. The onset was in April 1942. The sputum was negative; the vital capacity, 97 per cent; the Kahn test, negative. Laryngeal tuberculosis was diagnosed on Feb. 15, 1943, ulcerative, superficial, involving the arytenoids. The larynx was healed on May 26.

Case 3.—F. R., a Negro aged 21, had a diagnosis of far advanced pulmonary tuberculosis. The onset was in October 1943. The sputum was positive; the vital capacity, 49 per cent; the Kahn test, negative. Laryngeal tuberculosis was diagnosed on May 20, 1944, ulcerative. The larynx was inactive on June 8.

Case 4.—G. T., a white person aged 45, had a diagnosis of moderately advanced pulmonary tuberculosis. The onset was in February 1943. The sputum was positive; the vital capacity, 72 per cent; the Kahn test, negative. Laryngeal tuberculosis was diagnosed on December 2, granuloulcerative. The larynx was inactive on Feb. 1, 1945.

Case 5.—T. S., a white person aged 30, had a diagnosis of far advanced pulmonary tuberculosis. The onset was in March 1943. The sputum was positive; the vital capacity, 66 per cent; the Kahn test, negative. Laryngeal tuberculosis was diagnosed on Feb. 6, 1944, ulcerative. The larynx was healed on September 14.

Case 6.—L. H., a Negro aged 28, had a diagnosis of moderately advanced pulmonary and extensive bronchial tuberculosis. The onset was in October 1943.

The sputum was positive; the vital capacity, 32 per cent; the Kahn test, negative. Laryngeal tuberculosis was diagnosed on June 15, 1944, granuloulcerative. There was marked improvement on Jan. 25, 1945. At present this patient's condition is rapidly regressing due to the obstructive bronchial disease of the left main bronchus.

COMMENT

A casual review of the older as well as the more recent contributions in the literature devoted to this subject will reveal that there are many more therapeutic suggestions than those mentioned; these have not been considered here inasmuch as their value is largely historical and they contribute little if anything to the modern picture of successful laryngeal therapy. The divergence of opinion as to the best method of attack forces one to resort to the trite conclusion that while each has its limited place, no one method is worth consideration as the ultimate therapeutic answer.

Only a few years ago the complications of tuberculosis which occurred in the field of otolaryngology were in the hands of the phthisiologists. In the past decade more attention has been given to these complications by those who should be better qualified to handle them, the otolaryngologists. The obvious relationship between the upper and the lower air passages should suggest a similar association between those who render service to them. Certainly, the upper air passages should at no time be considered as a separate unit either by precedent or by the demarcation of specialization. The tabulation of the incidence of complications in itself should be of considerable aid to the internist when he is taking inventory of his past therapeutic results. The cases enumerated in the foregoing pages lay emphasis on the fact that the most important method of attacking laryngeal tuberculosis is pulmonary control; the very fact that laryngeal tuberculosis is always secondary to pulmonary tuberculosis lends credence to this statement. The success observed when laryngologic involvement is treated by the enumerated methods must be attributed to or shared with adequate collapse measures in a greater measure than has been heretofore generally realized.

A gradual decline in the incidence of extrapulmonary tuberculosis should be considered as mute testimony of greater diagnostic and therapeutic skill in pulmonary therapy. By the same token, the fact that laryngeal tuberculosis can show resolution under rest alone speaks eloquently for modern collapse methods and for those who administer them. It is by no means felt that all patients with laryngeal tuberculosis should rely solely on collapse methods for total therapeutic support. Rather, I wish to point out a therapeutic synergism as well as the need for cohesion in therapy of the upper and the lower respiratory system in tuberculosis.

PENICILLIN EAR DROPS IN THE TREATMENT OF SUPPURATIVE OTITIS MEDIA

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THE TREATMENT of infections of the middle ear frequently presents a problem both to the general practitioner and to the specialist. Because of the prevalence of suppurative otitis media and its wide distribution, any treatment which might safely result in a cure of the disease in the shortest possible time is worthy of trial. The treatment of aural infections with ear drops has long been standard. In recent years the use of sulfonamide drugs has been widespread in an attempt to shorten the duration of the disease. Opinions as to the efficacy of this treatment have varied. It has been praised as a short cure for suppurative otitis media and has been decried as a masker of complications of this disease. The use of sulfonamide compounds is always accompanied by the possible development of specific sensitivity, manifested by cutaneous eruptions or blood dyscrasias. There is also the possibility of renal block which must be kept in mind when using sulfonamide drugs. While these untoward effects are not frequent, they are encountered sufficiently often to put the physician on permanent guard against their development. Reports of the effectiveness of sulfonamide drugs in suppurative otitis have varied. Because of the absence of a reference library in an overseas installation, a review of this subject, with bibliography, is unfortunately unobtainable. However, it may be safely stated that any treatment which could provide the benefits of treatment with sulfonamide drugs—rapid cessation of the discharge—and avoid the difficulties would be an improvement. To this end it was decided to treat a series of unselected patients for purulent otitis media with penicillin drops. As control, a consecutive series of patients treated with boric acid–alcohol drops was studied and the pertinent data were recorded. All patients were young adult men in the armed forces overseas.

A comparison was made of the time required to cure the otitis media in each series. By the term cure is meant that hearing became normal and there was no discharge or recurrence of discharge, with the drum membrane becoming normal four to five days after cessation of the discharge. Because every patient with acute infection of the ear was seen within the first week of the disease, and because the onset of discharge is not easy to determine with complete accuracy in all

cases, the time required to cure the aural disease is recorded as the duration of treatment after admission to the hospital, which is in all cases the time at which treatment was begun. The end point recorded is that at which the ear became and remained dry, with no perforation, and asymptomatic. In no case labeled as cured was there a recurrence of the discharge. If this occurred, the time required to obtain a cure is recorded as that required to obtain a permanently dry ear.

There is a further subdivision into acute suppurative, traumatic suppurative and chronic suppurative infections. Because of the different characteristics of these types of aural infection, they are considered separately. The patients with acute otitis media all had an acute onset of earache, followed by discharge, with no previous history of aural complaints or disease for at least two years prior to the onset of the present episode. The patients with traumatic otitis all were battle casualties, their drums ruptured by shell, bomb or mine explosion or muzzle blast, with suppuration following rupture. The patients with

TABLE 1.—*Distribution of Cases in Two Treatment Series*

	Boric Acid–Alcohol Drops	Penicillin Drops	Total
Acute suppurative otitis media.....	24	19	43
Chronic suppurative otitis media.....	15	10	25
Traumatic acute suppurative otitis..	13	6	19
Total.....	52	35	87

chronic otitis media all had either continued aural suppuration for a period of a year or more or gave a history of an ear discharging at frequent intervals over a period of years. Table 1 shows the distribution of cases in the various groups described.

OBSERVATIONS ON EARS TREATED WITH BORIC ACID–ALCOHOL DROPS

Between Jan. 1 and Oct. 1, 1944 52 patients with suppurative otitis media were treated with boric acid–alcohol drops. All were in the hospital during the entire course of treatment. In each instance the external auditory canal was cleansed and boric acid–alcohol instilled into the ear three times a day. Of these 52 patients, 24 had acute suppurative otitis media, 15 chronic suppurative otitis media and 13 traumatic acute suppurative otitis media. All patients with traumatic otitis media had been treated with sulfonamide compounds in varying dosages, as this treatment was given routinely to all battle casualties in forward treatment areas.

Acute Suppurative Otitis Media.—Of the 24 patients with acute suppurative otitis media, 8 had been treated with sulfonamide drugs before admission and 16 had had no prior medication. The exact

dosages are unfortunately not known. These 8 treated patients were referred to this hospital because of the lack of response to the sulfonamide drugs. All 24 patients were treated with boric acid–alcohol drops. The periods of time required to obtain cures are shown in chart 1*A*. Each square represents 1 case. It may be seen that there is a concentration of cures at the two week period. An average treatment period of 17.4 days was required. This is shown also in table 2. There was no difference in the period of treatment required for the ears of patients who had previously been treated with sulfonamide compounds. In 2

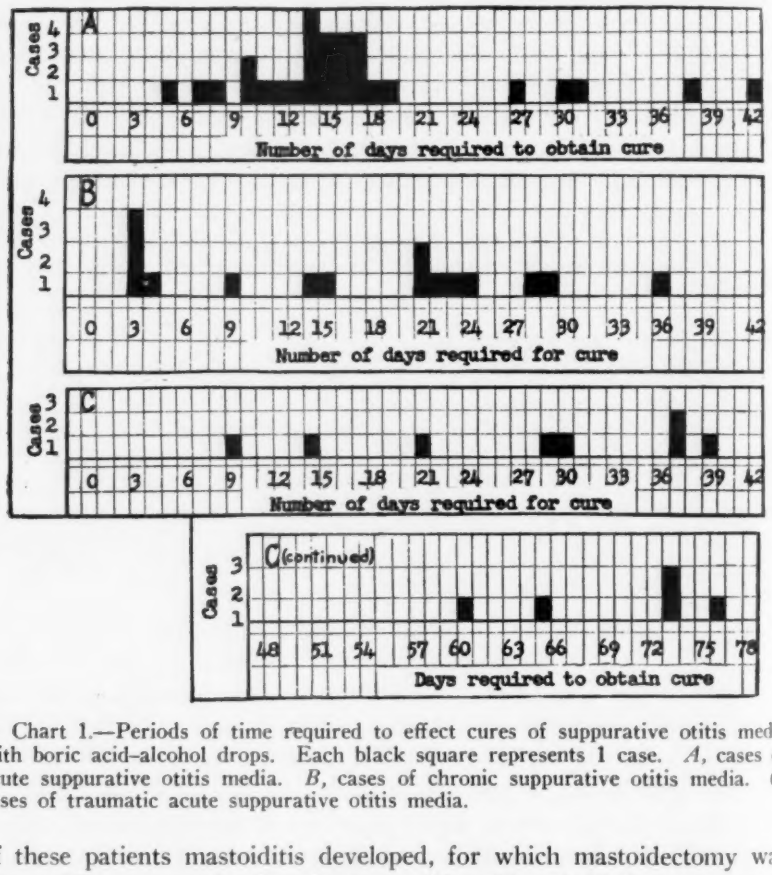

Chart 1.—Periods of time required to effect cures of suppurative otitis media with boric acid–alcohol drops. Each black square represents 1 case. *A*, cases of acute suppurative otitis media. *B*, cases of chronic suppurative otitis media. *C*, cases of traumatic acute suppurative otitis media.

of these patients mastoiditis developed, for which mastoidectomy was done. These were the 2 patients requiring 38 and 42 days treatment, respectively.

Chronic Suppurative Otitis Media.—Fifteen patients had chronic suppurative otitis media. All had dry ears after treatment with boric acid–alcohol drops. Chart 1*B* shows the time required for each cure. The average was 17 days, the same as for acute otitis media. However, there is no bunching of cures as in chart 1*A*. There is no duration of

treatment which might be considered as standard or expected. This is not strange, as there is a wider range of variability in the duration and the severity of chronic as compared with acute otitis media.

Traumatic Acute Suppurative Otitis Media.—Thirteen patients with traumatic acute suppurative otitis media were treated with boric acid–alcohol drops. Chart 1*C* shows the time elapsed before each of these patients was cured. Again, because of the greater variation in the severity and the cause of the traumatic disease, no concentration of cures at any given period is found. The average time to cure these ears was 38 days, as shown in table 2.

OBSERVATIONS ON PENICILLIN-TREATED EARS

The next series of patients was treated during the period Oct. 1, 1944 to April 1, 1945. This series is exactly comparable with the first, as all were members of the armed forces stationed in the same area. The decision to apply penicillin locally rather than to inject it into a muscle for circulatory distribution was prompted by the greater ease of administration. Furthermore, while intramuscular injection is practicable in an army hospital, it is highly unsatisfactory if one is treating a comparable group of ambulatory civilian patients. A solution of a penicillin salt prepared in isotonic, solution of sodium chloride with a strength of 1,000 Oxford units per cubic centimeter was used. No attempt was made to keep the solution refrigerated because of the discomfort of instilling a cold solution into the ear. Solutions up to a week old were used. No loss of response was noted when the old solutions were instilled. This is in contradistinction to the common usage of employing only refrigerated penicillin solution not over twenty-four hours old. The penicillin drops were administered three times daily, and a cotton wick was placed in the canal after each treatment.

Acute Suppurative Otitis Media.—Nineteen patients with acute suppurative otitis media were treated with penicillin ear drops. Sixteen had had no medication prior to admission to this hospital. Three had been treated with sulfonamide drugs or with penicillin intramuscularly injected or with both, with no benefit obtained. Chart 2*A* shows the periods of time required for cures in this group. Fifteen of the 19 patients were cured in 3 to 5 days. None of these patients had a recurrence of aural discharge or other symptoms. All had normal hearing and normal drums when discharged from the hospital. All were retained for observation for at least a week after the ear became dry, and most were followed as outpatients for considerably longer. In an overseas installation it is impossible to follow all patients for long, as they move into other areas. Two of the patients were cured in 10 days. One required 26 and another 30 days. The patient requiring 30 days had acute otitis media coincident with severe infectious hepatitis.

The one requiring 26 days had external otitis of an eczematoid type complicating the otitis media. When first seen he was found to have both external otitis and otitis media. The external otitis was treated with alcohol packs for 3 days and subsided. Following this, the penicillin drops were used for 3 days, and the ear became dry. During the next week, while he was under observation, the external otitis again became active, and 10 days after the ear first became dry the otitis media

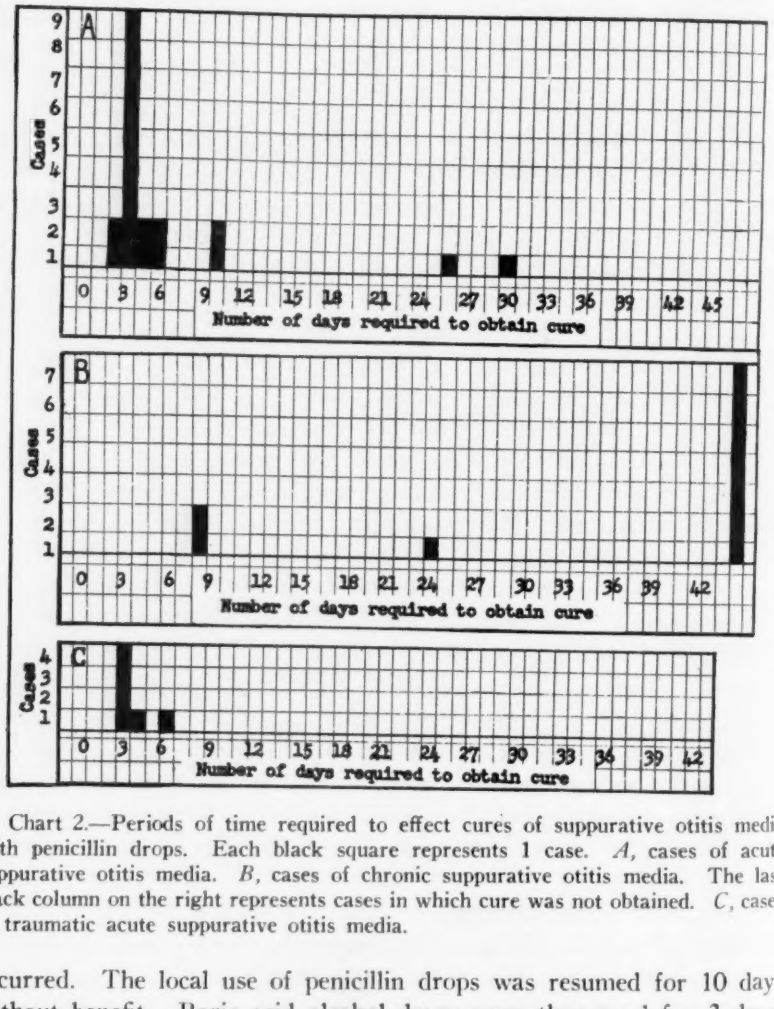

Chart 2.—Periods of time required to effect cures of suppurative otitis media with penicillin drops. Each black square represents 1 case. *A*, cases of acute suppurative otitis media. *B*, cases of chronic suppurative otitis media. The last black column on the right represents cases in which cure was not obtained. *C*, cases of traumatic acute suppurative otitis media.

recurred. The local use of penicillin drops was resumed for 10 days without benefit. Boric acid–alcohol drops were then used for 3 days, with a dry ear resulting. There was no further recurrence. There were no instances of mastoidal involvement or other complication in this group. The average time elapsed before cure was 6.8 days. Chart 2*A* shows that the great majority were cured with 3 days' treatment.

Chronic Suppurative Otitis Media.—Ten patients with chronic suppurative otitis media were treated with penicillin drops. Chart 2*B* shows the results in this group. Seven patients failed to get dry ears. Two were free from aural discharges after 8 days' treatment and a third after 24 days. Because of the varied factors involved, several cases will be discussed.

1. A man had a history of multiple recurrences of aural discharge of both ears since 1917. There were three episodes of otitis media on the left side in the six months prior to admission. He was first treated by his unit medical officer with sulfadiazine, 1 Gm. every four hours for 4 days, without beneficial results. He was then admitted to this hospital. The hearing was 15/15 in each ear. There was an anterior inferior perforation of the left drum membrane with a thin purulent discharge. Penicillin drops were administered three times daily for 21 days. The discharge became less but never stopped. Then boric acid–alcohol drops were used, and the ear became dry in 3 days, and stayed dry. This sequence was seen several times in the patients with chronic otitis media.

2. A patient had continued purulent discharge from the right ear since early childhood. There was a posterior superior perforation of the right drum membrane with profuse foul purulent discharge. Hearing was 2/15 in the right ear and 15/15 in the left. Roentgenograms of the mastoid process revealed a large cholesteatoma of the right process. Penicillin drops were used for 18 days, with no change noted in the aural infection. In aural disease of this type, with destruction of bone and extensive inflammatory changes, it is not surprising that conservative management yields no results. The penicillin drops were ineffective.

3. A man had continued purulent discharge from the left ear since 1937. Examination showed 3/15 hearing in the left ear and a marginal perforation with a large aural polyp. The polyp was removed. Penicillin drops were used for 35 days. The discharge lessened but never stopped completely. Again, in the presence of old persistent aural infection the penicillin was ineffective.

4. A patient had discharge from the left ear continuously for one year. He had been treated with boric acid–alcohol drops, with sulfadiazine, and with penicillin, intramuscularly injected, before admission to this hospital. The hearing in the affected ear was 12/15. There was an anterior inferior perforation with a thin purulent discharge. There was also external otitis of an eczematoid type. As in the patient with acute otitis media described, the external otitis was treated with alcohol packs for 3 days, with marked improvement. After 3 days' treatment with penicillin drops, the ear became dry. Again, after the lapse of a week both the external otitis and the otitis media recurred. Penicillin drops were then ineffective.

5. A man had continued discharge from the left ear since 1937. There was an anterior inferior perforation of the drum membrane with a large polyp. Polypectomy, penicillin drops and boric acid-alcohol drops all failed to dry the ear.

The cases mentioned illustrate the type of aural disease which did not respond to penicillin drops. The experiences in treating such patients suggested that chronic otitis media be treated with penicillin drops for 3 days and then with boric acid–alcohol drops. The combination when tried appeared to be superior to either medication used alone.

Traumatic Acute Suppurative Otitis Media.—Six patients with traumatic otitis media were treated with penicillin. The involved ears all cleared up within six days after the administration of the drops was begun. Four patients were cured in 3 days. Two were cured in 4 and 6 days respectively. Chart 2*C* shows the period of time required in each case. No complications or recurrences were noted.

SUMMARY AND CONCLUSIONS

In table 2 a comparison is made between the average time required to cure infections of the middle ear with boric acid–alcohol drops and that required to cure such infections with penicillin drops.

TABLE 2.—*Average Periods of Time Required to Cure Suppurative Otitis Media with Boric Acid–Alcohol and Penicillin Drops, Respectively*

	Boric Acid–Alcohol Drops	Penicillin Drops
Acute suppurative otitis media	17.4 days	6.8 days
Chronic suppurative otitis media	17.0 days	No benefit obtained
Traumatic acute suppurative otitis	38.0 days	3.7 days

The following conclusions may be drawn:

1. Penicillin drops, 1,000 Oxford units per cubic centimeter, offer a safe, rapid and effective treatment for acute suppurative otitis media. In this series they were far more effective than boric acid–alcohol drops.
2. Penicillin drops offer a treatment for suppurative aural disease which is free from the potential dangers of sulfonamide medication. No complications due to the use of penicillin were encountered.
3. Penicillin ear drops are essentially ineffective in treating old chronic suppuration of the ear. However, when they are used in combination with boric acid-alcohol drops beneficial results may be obtained.
4. Penicillin drops should be used with caution in the presence of external otitis.

It is believed that the results shown in this small series warrants further use of penicillin drops in treating suppurative otitis media, both for the benefits obtained and for the purpose of securing further data from observation of more cases and different types of cases.

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HYPERTROPHY OF THE MASSETER MUSCLE

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THE masseter muscle originates on the zygomatic arch and the zygomatic process of the maxilla and is inserted into the lateral aspect of the angle and ramus of the mandible. When the muscle is activated by a clenching of the teeth, its belly can be seen bulging under the skin, and the anterior edge may easily be palpated in the substance of the buccal wall. In a gaunt subject or in one whose mandibular angles flare outward the masseter muscles may be prominent.

At times the prominences may be such that the subject will seem to have bilateral swellings of the jaw, and epidemic parotitis will be suspected. This has occurred several times during routine examinations of troops for communicable diseases and has resulted in unwarranted hospitalizations and isolations. In each instance in which this occurred, a story of habitual clenching of the jaws repeatedly when emotionally disturbed or under nervous tension was elicited from the patient. In these cases the condition was interpreted as simple hypertrophy of the muscle and was readily distinguishable by location and by history from parotitis.

When the hypertrophy occurs unilaterally its appearance is more striking because of the resultant facial asymmetry. To date, 5 soldiers have been observed who presented themselves with the complaint of a lump or tumor on their jaws. These masses were painless, of indefinite origin and had been noticed only because the patients' attention had been directed to them by questionings of their fellow soldiers or by medical officers.

REPORT OF CASES

CASE 1.—A white soldier aged 21, in service for four months, had had his attention attracted to a swelling of his right cheek four weeks before. The mass was painless; he thought that it was getting larger, but he had not noticed it previously.

Examination on March 16, 1943 revealed an enlargement over the angle of the right side of the jaw extending from the ear lobe anteriorly for about 3 cm. and from the lower border of the mandible superiorly for about 4 cm. There was no definite outline; it was doughy in character and apparently solid. Activation of the muscles of mastication by clenching of the jaw caused the mass to protrude more prominently. Aspiration of the mass revealed nothing.

It was felt that, because of the unusually great size of the mass and because of the short time since it had been noticed, a neoplasm was present, and a pre-

sumptive diagnosis of (1) lipoma or (2) rhabdomyoma of the masseter muscle was made.

Accordingly the skin was incised and the fascia split over the prominence to expose the tumor. It was then seen that the entire mass was due to a normal-appearing but thick masseter muscle. A finger was inserted into the mouth to push the cheek out, and it was clearly demonstrated between the internal and the external palpating finger that only muscle was present. To prove further that no tumor was being overlooked, a blunt hemostat was inserted into the muscle belly to tease the fibers apart through the entire thickness of the muscle up to the buccal mucosa. Normal muscle tissue was found throughout.

The wound was closed, and healing was uneventful.

Postoperatively the patient was questioned regarding his chewing habits, and he revealed that whenever he was under any sort of mental stress he worked his jaws by clenching his teeth and wriggling his cheek muscles. In doing this he moved the right side more, although his occlusion was normal.

CASE 2.—On Nov. 22, 1943, a 20 year old white soldier, in service for seven months, was referred to the ear, nose and throat clinic with the diagnosis of a parotid tumor. He had been told by his friends two weeks before that he had a lump on his jaw. He did not know how long it had been there and experienced no discomfort from it.

Inspection revealed a definite prominence on the left side over and anterior to the angle of the jaw. It was nontender, doughy in character and not attached to the skin, and it seemed to merge with the masseter muscle. When the latter was activated, it was clearly revealed that the mass was actually the bulging belly of the muscle. Contraction of the muscle caused the mass to become firmer, knotted and more prominent.

This patient was not questioned regarding his chewing habits, but it was noted that his articulation was normal.

CASE 3.—On Nov. 25, 1943, a 32 year old white soldier, in service for twenty-two months, presented himself with the complaint of a pain in the left side of his forehead which had started five days before and which had caused him to notice for the first time that there was a "marked swelling" of the left side of his jaw. Because he had never previously noticed this, he presumed that it was of only a few hours' duration and was associated with the pain in his forehead.

Examination revealed that the belly of the left masseter muscle was prominent and that on activation it became hard, knotted and more prominent. The patient in addition had a high left deviation of the nasal septum with impaction on the left side of the middle turbinate and had a middle meatus that was packed with polyps. It was felt that these rhinologic findings accounted for the headaches.

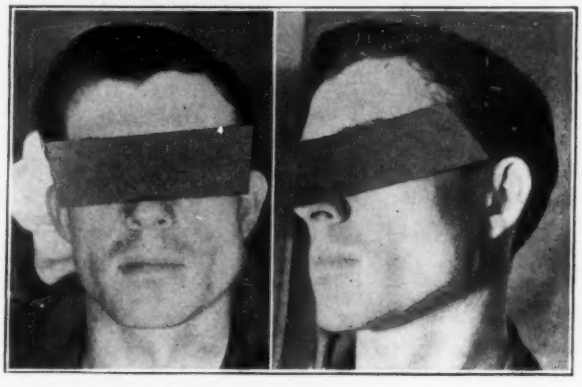
CASE 4.—On Dec. 11, 1944, a 22 year old Negro soldier, in service for eighteen months, presented himself with the complaint of a swelling in the left side of his jaw. During a routine check-up for contagious disease the patient was asked by the medical examiner about the swelling of his jaw, and this was the first time that his attention had been directed to it. He was a tense, tremulous and apprehensive man and during the questioning was seen to clench his jaws and to activate the left masseter muscle more than the right one.

Examination of the "tumor" mass revealed it to be only an excessively developed masseter muscle in a subject whose mandibular angles flared outward. This outward flare and the colored skin caused the bulge to be noticeable on that side so that, in effect, the patient did resemble a person with unilateral

epidemic parotitis. His temperature was normal, as were his white blood cell count and white blood cell differential count. The "mass" was nontender, and the orifice of Stensen's duct was normal. All the right lower molar teeth were missing.

CASE 5.—On April 20, 1945, a 25 year old white soldier, in service for seventeen months, was referred to the ear, nose and throat section because of a mass in the left side of his jaw. This mass was first noticed three weeks previously, when another soldier questioned him about it. He believed, since he had not noticed it, that it was recent in development, and he had fretted so much and fingered the jaw so frequently that, he claimed, during the past week it had ached intensely.

Inspection revealed a definite protrusion over the left side of the mandible, from the angle forward for 3 cm. (figure). The "mass" was doughy in character, unattached to the skin and absolutely painless. Activation of the masseter muscle displayed that the mass was merely the belly of the muscle and changed its character from doughy to firm.



Close-up views of patient, showing hypertrophy of the left masseter muscle (photographs by United States Army Signal Corps).

The occlusion was normal, and clenching of the jaw and habitual grinding of the teeth were denied. The patient did volunteer the fact that he did most of his chewing on the left side of the mouth. After the benign nature of the bulge was explained to the patient, he was reassured, and the "pain" disappeared.

COMMENT

The differential diagnosis is the most important consideration when hypertrophy of the masseter muscle exists, particularly when it is unilateral and results in facial asymmetry. Parotitis, parotid neoplasms (especially mixed cell tumors), sebaceous cysts and lipoma must be considered.

Parotitis, epidemic or otherwise, is usually readily differentiated by the history of sudden onset, by the presence of pain, by the blood count, by the reddening of the orifice of Stensen's duct and finally, in the case of the epidemic type, by the elevation of the level of serum amylase.

Activation of the masseter muscle in these cases in no way changes the character of the mass nor does it cause the mass to protrude farther. In fact, all of the enlargements resulting from change in the parotid gland tend to be located nearer to the lobe of the ear than the bulging masseter belly.

Clinically a mixed cell tumor of the parotid gland is usually an encapsulated mass in the gland and is fairly sharply defined on palpation. It may be cystic in nature but generally is firm and lobulated. The malignant tumors usually have a history of sudden rapid growth, may be attached to the skin, blend with the parotid gland and are accompanied by enlargement of the tributary lymph nodes.

A sebaceous cyst in this region is not uncommon, but because of its superficial location in the skin it should not offer any great difficulty in the determination of its true nature.

Lipomas around the mouth and jaws are uncommon. Padgett [1] mentioned a congenital lipoma arising in the canine fossa, internal to the masseter muscle, which might be mistaken for a parotid tumor. Lipomas, wherever located, are subcutaneous and have a soft elastic feel. This persists even if an underlying muscle is activated. In the cases cited in the present article the tumor mass became firm and hard when the muscle was activated, and in the 1 case in which the mass was explored it was seen to be merely the muscle belly. Of course, in cases in which the nature of the enlargement is doubtful even after observation, surgical exploration may prove to be the only reliable means for making a diagnosis.

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1. Padgett, E. C.: Surgical Diseases of the Mouth and Jaws, Philadelphia W. B. Saunders Company, 1938.

EVALUATION OF BENADRYL AS A THERAPEUTIC AGENT FOR VASOMOTOR AND ALLERGIC RHINITIS

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THE ideal drug has not been found which will alleviate the uncomfortableness of the nasal congestion associated with vasomotor and allergic rhinitis until the causative factors can be eliminated or permanently controlled by other measures. The local use of ephedrine or ephedrine-like preparations is of value but gives relief for short periods only. Many such drugs produce subsequent vasodilatation and nervousness if used too frequently, and they tend to lose their effectiveness if constantly used for long periods. Preparations belonging to this group must be used rather cautiously in hypertensive patients and patients with cardiac disease.

When persons seek advice for nasal congestion and its associated complaints, the rhinologist must attempt to give them temporary relief while the investigation to determine the etiologic factors proceeds. Since the investigation is often time-consuming, with laboratory studies, allergy studies and consultations, palliative measures are necessary until the rhinologist can definitely determine the proper therapeutic regimen to follow. Even after treatment has begun, several weeks may elapse before the patient receives substantial benefit, whether it is by elimination of the allergens, desensitization, correction of metabolic disturbances, intraturbinal injection of sclerosing agents or other measures used in the vasomotor group.

The present concept of allergy is that allergens produce on sensitized cells an effect causing liberation of histamine or of a histamine-like substance which initiates the symptoms recognized as allergic manifestations. Consequently, it is rational to work on the hypothesis that the administration of antihistaminic substances should have a beneficial effect in relieving the symptoms associated with hypersensitivity. A new antihistaminic drug, reported by Loew and associates,[1] stimulated this

From the Carle Clinic.

1. Loew, E. R.; Kaiser, M. E., and Moore, V.: Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, J. Pharmacol. & Exper. Therap. **83**:120, 1945. Loew, E. R., and Kaiser, M.: Alleviation of Anaphylactic Shock in Guinea Pigs with Synthetic Benzhydryl Alkamine Ethers, Proc. Soc. Exper. Biol. & Med. **58**:235, 1945.

clinical investigation. Their research with synthetic benzhydryl alkamine ethers revealed that beta dimethylaminoethyl benzhydryl ether hydrochloride, designated Benadryl, was the most effective antihistaminic preparation studied in alleviating anaphylactic and histamine shock in animals. It was effective in much smaller doses than theophylline ethylenediamine in relieving bronchial constriction and diminished the depressive effects of histamine and acetylcholine. They stated that this substance has very low toxicity. McElin and Horton [2] found that Benadryl decreased the cutaneous vasodilating effect of histamine and that it alleviated the nasal congestion induced by histamine. They stated that Benadryl depressed the gastric response to histamine and that this drug depressed the wheal and flare response in cases of hypersensitiveness to cold. Eight patients with vasomotor rhinitis were treated; 5 experienced excellent results, 2 were moderately relieved, and 1 received no benefit. They reported excellent relief in 19 of 22 patients with true hay fever, good results in 2, and failure in 1. The oral dosage varied from 50 to 500 mg. per day. They administered the drug intravenously in some of their patients, using 60 mg. per hundred cubic centimeters of isotonic solution of sodium chloride. McElin and Horton found no abnormal changes in the blood count, the blood platelet count, the bleeding and clotting times, the urea content or the results of urinalysis in the group studied. The most common side effects noted by them were sleepiness, dizziness, dry mouth and a feeling of nervousness. Koelsche, Prickman and Carryer [3] treated 83 patients with hay fever, bronchial asthma or both combined. Benefit was reported in 69 per cent of the total group studied. Only 33 per cent of patients with bronchial asthma alone were benefited (4 of 12). About 75 per cent of the persons with hay fever or asthma with hay fever in association claimed at least 50 per cent or more relief of their symptoms. Williams [4] reported that 10 of 12 patients with perennial vasomotor rhinitis obtained 90 per cent relief. He stated that the average patient with physical allergy of the head could be kept practically free of symptoms with 50 mg. of Benadryl given six times daily (300 mg.). Logan [5] reported good to excellent results in 9 of 12 children

2. McElin, T. W., and Horton, B. T.: Clinical Observations on the Use of Benadryl: A New Antihistaminic Substance, Proc. Staff Meet., Mayo Clin. **20**:417, 1945.

3. Koelsche, G. A.; Prickman, L. E., and Carryer, H. M.: The Symptomatic Treatment of Bronchial Asthma and Hay Fever with Benadryl, Proc. Staff Meet., Mayo Clin. **20**:432, 1945.

4. Williams, H. L.: Use of Benadryl in the Syndrome of Physical Allergy of the Head: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **20**:434, 1945.

5. Logan, G. B.: The Use of Benadryl in Treating Some of the Allergic Diseases of Childhood, Proc. Staff Meet., Mayo Clin. **20**:436, 1945.

with hay fever. He expressed the belief that 2 mg. per pound of body weight is an adequate dose in most instances.

PROCEDURE

All patients were thoroughly investigated. The history was taken, and a complete physical examination was made, with routine laboratory work, besides nasal smears for eosinophilia, cutaneous tests for allergy and roentgenograms. Consultations were requested from the other specialists of the clinic in order to rule out all organic disorders except the allergy and vasomotor rhinitis not due to discoverable allergens. All patients studied in this series complained of year round (perennial) symptoms. No patients with true seasonal allergic rhinitis were included in the investigation. Five of the allergic patients with multiple sensitivities had been following an allergy regimen for four months with only partial relief. The remainder of the group were given Benadryl for a time, and then procedures for control of allergy were instituted, after the effect of the Benadryl had been determined. The daily intake of Benadryl varied from 150 to 400 mg., given in 50 to 100 mg. doses. The frequency of administration ranged from three times daily to every three hours. The use of the drug was then discontinued to see whether symptoms returned. After two weeks had elapsed, the patients resumed the Benadryl therapy for a period to see whether the symptoms would again be alleviated. Since persons with vasomotor and allergic rhinitis tend to have periods when their nasal symptoms are less severe, this procedure was instituted in order to have a double check on the efficacy of this antihistaminic preparation.

RESULTS

The results have been tabulated into three categories: (1) complete relief of symptoms with abatement of the physical findings previously noted; (2) definite symptomatic improvement, with the nasal congestion and abnormal secretion found to be definitely reduced on inspection; (3) questionable improvement in one or two of the symptoms but no appreciable change in the appearance of the nasal membranes; in this category also was absence both of symptomatic improvement and of change of appearance of the mucous membrane.

Patients classified as having vasomotor rhinitis met the following requirements:

1. There had been intermittent nasal congestion, bilateral or alternate, for one or more years.
2. The mucosa of the turbinates appeared normal or, if redder than normal, showed little or no excessive nasal secretion.
3. The engorged turbinates shrank well after the use of ephedrine-like preparations.
4. The history was negative for allergy, the nasal smears showed no eosinophilia and cutaneous tests revealed no allergens.

The more thoroughly vasomotor rhinitis is studied over a long period, the more convinced one becomes that in some of the cases at least there are early manifestations of intrinsic or extrinsic allergy but the disease is not far enough along to be classified as such.

Twenty patients were classified as having vasomotor rhinitis; complete relief of symptoms occurred in 30 per cent and definite improvement in 20 per cent during Benadryl therapy. Forty-two patients had nonseasonal perennial allergic rhinitis; complete relief of symptoms was obtained in 28.5 per cent and definite improvement in 14.3 per cent, whereas 57.1 per cent received little or no benefit from taking Benadryl. Only one half of the few patients with nasal allergy and associated bronchial asthma were benefited, and none of these were completely relieved of their symptoms. The dyspnea was improved about 50 per cent or more, expectoration was easier and the asthmatic attacks were less severe.

One patient with an associated pseudo or early form of Ménière's syndrome obtained an excellent result. A second patient with a syndrome of this type was not improved after the Benadryl treatment.

TABLE 1.—*Results of Benadryl Therapy in Seventy-Two Patients with Vasomotor and Perennial Allergic Rhinitis*

	Vasometer Rhinitis		Perennial Allergic Rhinitis		Allergic Rhinitis with Asthma		Associated Pseudo Ménière's Syndrome	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Total Group Percentage
Complete relief..	6	30	12	28.5	..	..	..	25
Definite improvement..	4	20	6	14.3	4	50	1	20.8
Slight or no benefit.....	10	50	24	57.1	4	50	1	54.1
Total number of patients....	20	..	42	..	8	..	2	..

Of the total number of patients treated in this rather small series, 25 per cent obtained complete relief and 20.8 per cent definite improvement, whereas 54.1 per cent received no benefit.

The nasal smears of 77 per cent of the allergic patients demonstrated eosinophilia, the counts varying from 15 to 90 per cent.

Symptoms returned after discontinuance of the use of Benadryl, even though some patients received the drug for two months. This is what one would anticipate, since there is no evidence that this drug has any ability to desensitize or form a permanent bond or combination with cellular structures to prevent a return of allergic symptoms due to liberation of histamine after withdrawal of the Benadryl. In some way, not well understood at present by pharmacologists and physiologists, Benadryl has a temporary antihistaminic effect, suggestive of antagonism, of neutralization or of combination with cellular receptor, thereby preventing anaphylactic and histamine reactions. Whatever the mode of action, and it cannot be so simple, it remains for further investigations to explain why the symptoms of some patients are relieved, and those of others are not, by such antihistaminic drugs.

A review of a few of the cases in which benefit was received may be of value in helping others to determine those types of patients in whom benefit may be anticipated, and may stimulate interest in furthering therapeutic investigation of the allergic problems associated with the otorhinolaryngologists' specialty.

REPORT OF CASES IN WHICH BENADRYL GAVE RELIEF

W. B., a white woman aged 32, had as chief complaints intermittent nasal obstruction, sneezing and much watery secretion. She had suffered from these for about four years. Other symptoms of shorter duration included fatigue, "gas on the stomach" and generalized headache. The turbinates were paler than normal and were turgescent with a good deal of mucoaqueous secretion from the nose. The sinuses revealed mild edema of the mucosa. Nasal smears showed 20 per cent eosinophils. Cutaneous tests for allergy showed the patient to be sensitive to house dust and tobacco. The general physical examination, including roentgen study of the gallbladder and the gastrointestinal tract, revealed nothing abnormal. She was treated with 50 mg. of Benadryl four times daily for two weeks, during which time she became free of nasal congestion, sneezing, excessive nasal secretion, headaches and "gas on the stomach." Then this therapy was stopped for two weeks, and the symptoms returned. The therapy was resumed for a period, during which her symptoms again disappeared. Then an allergy regimen was started. Slight drowsiness was noted during the first two days when she took Benadryl. Some dryness of the mouth persisted during the treatment with the drug.

W. M., a white woman aged 36, complained of nasal congestion, some sneezing and postnasal dripping the year round. She had been under observation for one year. The turbinates were of the vasomotor type. No eosinophils were present in the nasal smears. Cutaneous tests for allergens were negative. General physical examination revealed no apparent cause for the vasomotor rhinitis. She was given 50 mg. of Benadryl four times daily. One week later there was only an occasional spell of sneezing, and her nose was staying open well. The nasal membranes were definitely improved on inspection. The drug was not taken for two weeks, during which time her symptoms again became aggravated. When the therapy was resumed, the symptoms again improved. She noticed two side effects from Benadryl: dizziness and nervousness. The dose has been reduced to 50 mg. twice daily, which continues to give her moderate relief, with absence of the side effects.

J. M., a married woman aged 50, had as her chief complaint dizziness which had been present for over three months, especially marked on sudden change of the position of the head. She had also noticed diarrhea, eight to ten stools daily, for the same period and some gastric disturbance. Moderate intermittent nasal congestion had been present for about two years. Nasal smears showed no eosinophils; cutaneous tests for allergy were negative. Audiometric and caloric tests gave normal results. Complete physical examination and roentgenograms of the gallbladder, the gastrointestinal tract and the skull revealed nothing abnormal. All laboratory investigations, including agglutination tests and examinations of stools, did not give any leads as to diagnosis. A tentative diagnosis of vasomotor disturbance with probable pseudo Ménière's syndrome was made. The patient was given 50 mg. of Benadryl four times daily for one week. The

nasal congestion, the dizziness and the gastrointestinal disorder disappeared. The stools became formed and were reduced to one a day. Benadryl therapy was stopped for the next two weeks, and the patient was restricted to a sodium chloride–free diet. Potassium chloride and nicotinic acid were given by mouth during this two week period. The dizziness returned but was less severe than originally, and the stools became more frequent but still were formed. Benadryl therapy was resumed in the fourth week, and use of the other medicaments was discontinued. The dizziness and the nasal congestion again disappeared, and there was only one formed stool a day.

R. L., a youth aged 15, was first seen in October 1945, with chief complaints of asthmatic wheezing, rhinorrhea and nasal blockage, which had been present off and on since he was 6 years. There had been no seasonal variation. The nasal tissues were pale and edematous, with much watery secretion. Nasal smears showed 30 per cent eosinophils. There were many squeaky rales throughout the lungs. The sinuses transilluminated somewhat poorly. Roentgenograms of the chest showed nothing abnormal. Roentgenograms of the sinuses revealed some edema of the mucosa. Cutaneous tests showed the patient to be allergic to several inhalants and many foods. The blood was normal except for 14 per cent eosinophils in the differential count, the total white count being 7,400. Other laboratory tests gave normal results. An allergic regimen was instituted, and theophylline ethylenediamine and nadin (a proprietary water-soluble preparation of iodine) were given, with improvement for three months. In January 1946 the patient began having severe asthmatic attacks and nasal symptoms again. Benadryl in 50 mg. doses was given four times daily in February for one week. Marked improvement in the nasal and thoracic symptoms resulted. The Benadryl was withdrawn, and the symptoms returned, as well as the physical findings of allergic rhinitis and asthma. Treatment with Benadryl was resumed in March, 50 mg. being taken at breakfast, 50 at noon, 50 at 4 p. m. and 100 at bedtime. Larger doses produced dizziness and "dopey feeling." Since that time he has noticed little nasal disease and no asthmatic attacks. Inspection of the nasal tissues reveal them to be markedly improved. Even though no asthmatic attacks have been noticed by the patient, there is still an occasional rale heard in the chest.

C. L., a girl aged 10, weighing 75 pounds, complained chiefly of nasal obstruction, sneezing, watery discharge and recurrent attacks of urticaria and eczema. She had adhered to a regimen for control of allergy two years with little benefit. Cutaneous tests revealed that she was sensitive to many inhalants and ingestants. The turbinates were pale and turgescent, and there was considerable watery secretion. The sinuses were slightly hazy to transillumination. Nasal smears revealed 20 per cent eosinophils and an occasional pus cell. The blood count was normal except for 8 per cent eosinophils in the differential count. Benadryl, in 50 mg. doses, was given at breakfast and at the noon and evening meals for ten days. Relief of the nasal congestion, sneezing and nasal secretion occurred. The use of the preparation was stopped for two weeks, and the symptoms returned. Benadryl therapy was then resumed. She has now been taking this medicament for one month. She has been free from sneezing and the watery nasal secretion. There is occasional slight nasal congestion, not severe enough for her to resort to the use of nasal spray or nose drops. The turbinates appear more normal, having lost the pale appearance of the mucosa and the boggy character. It is hard to say whether or not Benadryl was of any benefit in

preventing urticaria, since the patient had none when first seen and before the use of the drug was started. This patient did not notice any side effects while taking this preparation.

SIDE EFFECTS OF BENADRYL THERAPY

The most common side effect noted was drowsiness. This occurred in 39 per cent of the patients. It usually disappeared after the first day or so of administration, but 2 patients discontinued taking the drug because of this symptom (table 2). Dryness of the mouth was noticeable in 25 per cent but was not annoying enough to stop the use of the medicament. Some nervousness was noticed by 11 per cent, and in 2 patients it was necessary to reduce the intake of the drug to 50 mg. twice daily, which still moderately controlled the nasal symptoms. Dizziness, which was mild and transient, occurred in 7 per cent. Weakness and fatigue were noticed by 7 per cent. Epigastric distress annoyed 5.5 per cent. Diarrhea occurred in 2 patients who had taken the drug two or three days. The use of the drug was stopped for one week, and then resumed, and both of these patients had no further diarrhea. It is therefore questionable whether the Benadryl was the cause of the diarrhea. One third of the entire group had no side effects while taking this medicament. The blood count and the urinalysis remained normal in the cases in which tests were done; some of the patients had taken the drug for two months.

TABLE 2.—*Side Effects Noticed by Patients While Taking Benadryl*

	Number of Patients	Percentage of Patients
Sleepiness	28	39
Mild	26	..
Marked (stopped use of drug)	2	..
Dryness of mouth	18	25
Mild	14	..
Rather marked (use of drug not stopped)	4	..
Nervousness	8	11
Necessary to reduce dose	2	..
Dizziness	5	7
Weakness, fatigue	5	7
Epigastric distress	4	5.5
Diarrhea (questionable if caused by benadryl)	2	2.7
No side effects	24	33

SUMMARY

Benadryl was given to 72 patients whose complaints embraced vasomotor rhinitis, definite perennial allergic rhinitis and nasal allergy associated with asthma. Marked improvement or complete relief from nasal congestion and its associated symptoms occurred in 50 per cent of the group with vasomotor rhinitis and in 42.8 per cent of the group with perennial allergic rhinitis. Only 4 of the 8 patients with associated

asthma were definitely improved, with none of these obtaining complete subsidence of the thoracic symptoms and physical findings. One patient with pseudo Ménière's syndrome obtained complete relief; another was not helped. Of the whole group, 25 per cent obtained complete relief while taking Benadryl, and 20.8 per cent were definitely improved. Only very slight or no improvement was recorded for 54.1 per cent.

Benadryl [6] may be added to the list of drugs to be used in controlling temporarily vasomotor and perennial allergic rhinitis until the patients can be thoroughly studied and sound therapeutic procedures instituted to control permanently the vasomotor and allergic phenomena. The drug should not be given for a few days preceding cutaneous testing for allergy, because the effect may interfere with the wheal and pseudopodia formation in response to the allergens used. From this investigation it is concluded that a physician cannot expect more than one half of the people suffering from vasomotor and perennial allergic rhinitis to be benefited by the use of Benadryl. There is no evidence at present that withdrawal of this antihistaminic drug after prolonged administration will demonstrate a patient permanently relieved of his nasal and associated symptoms. Benadryl is certainly not the answer to the physician's prayer for a solution of the allergic problems which face him and his patients. However, it is another step forward in controlling that part of the vasomotor and allergic equation associated with liberated histamine.

6. Benadryl is a product of Parke, Davis & Company.

TREATMENT OF CHRONIC PURULENT OTITIS MEDIA WITH GLYCERITE OF HYDROGEN PEROXIDE

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AFTER the discovery by one of us (E.A.B.) that certain peroxides could be stabilized and their action prolonged, it occurred to the other (W.E.O.) that a solution of hydrogen peroxide in glycerin might be effective in the treatment of chronic purulent otitis media.

The solution, of which the stability,[1] the antiseptic properties[2] and the studies on tissue tolerance[3] have been described elsewhere, consists of hydrogen peroxide (1.5 per cent) derived from urea peroxide in anhydrous glycerin. When brought into contact with water, the urea peroxide is changed to urea and hydrogen peroxide. The peroxidase and catalase systems change hydrogen peroxide into water and oxygen. The peptizing action, healing effects and bacteriologic properties of urea are too well known to require further description.

Hydrogren peroxide has been used as an antiseptic for many years. Its chief disadvantages are, in vitro, its instability and, in vivo, its transient action. Its solution, however, in solvents of high viscosity stabilizes it and prolongs its action, the released oxygen being held in the gylcerin and acting at the interface between the tissues and the antiseptic. Its action is therefore prolonged.

The third constituent, glycerin, has itself been used as a vehicle for aural medication. Its hygroscopic properties enable it to reduce swelling. Its osmotic pressure draws plasma from the deeper parts of damaged tissues, acting to wash out particulate matter and subjecting it to both the antiseptic powers of the peroxide and the peptizing

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The Buffalo Electro-Chemical Corporation, Buffalo, and the International Pharmaceutical Corporation, Boston, supplied the material for experimental purposes.

1. Brown, E. A.; Abramson, H. A.; Gorin, M. H.; Kauffmann, H., and Shanley, E. C.: The Stability of Solutions of Urea Peroxide in Alcohols, to be published.

2. Brown, E. A.; Krabek, W., and Skiffington, R.: A New Antiseptic Solution for Topical Application, New England J. Med. **234**:60, 1946.

3. Brown, E. A.: Studies on Tissue Tolerance to a New Glycerol Peroxide Antiseptic Solution, Ann. Allergy **4**:33, 1946.

action of the urea. The high viscosity of the solvent keeps the medication where it is placed and therefore effective for long periods. In the absence of water there is no dermatitis of the type so often seen in the past with aqueous solutions of hydrogen peroxide.

The antiseptic solution has then the following properties which suggest that its use in aural infections would be worthy of trial. It is stable, nontoxic, nonirritating and nonallergenic. It is activated by blood or plasma to release oxygen which is held in situ, the clear liquid gradually turning into foamy emulsion. It therefore combines the advantageous properties of both the liquid and the ointment type of application. It is hygroscopic, peptizing and bactericidal. It acts on bacteria independently of their gram characteristics.[2]

The patients listed in the following paragraphs were treated in the office and at home and were instructed to use ½ dropperful of the solution in the ear every four hours from arising until retiring. In many cases, prior to the use of the antiseptic solution the ear was irrigated with a warm saturated solution of boric acid.

There were, in all, 37 patients. Of these, 2 failed to return for further treatment or observation and the results in their cases may be considered as failures. Of the remainder, 3 showed no improvement and, in addition, 3 were given or required penicillin administered intramuscularly or locally to clear their conditions. The chronic purulent otitis media of 29 patients completely cleared with the antiseptic alone. In no case did the solution cause local irritation. In 2 patients (F.E.H. and C.P.) the use of the drops was associated with nausea or vertigo. Both patients, however, persisted with their treatment until their conditions cleared.

Before using the glycerin peroxide solution, all the patients had been treated in the usual way, but ineffectively, with one or several of the following medications: boric acid; boric acid and alcohol; boric acid, alcohol and hydrogen peroxide; sodium sulfathiazole solution (5 per cent sulfathiazole); sulfanilamide; an iodine–boric acid powder; tyrothricin, or penicillin.

Bacterial cultures were taken immediately before treatment was initiated and at varying intervals thereafter. The bacteria, present alone or usually in mixed cultures, included Staphylococcus albus and Staphylococcus aureus, hemolytic and nonhemolytic streptococci, Escherichia coli, Bacillus proteus, diphtheroids, gram-negative bacilli and gram-positive micrococci. Cultures of material from the ear of 1 patient presented a growth of Aspergillus albicans and of another a growth of yeast cells. It should be noted that the list includes organisms which are nonsensitive to penicillin.

The ages of the patients varied from 3 to 65 years. The conditions of the patients had been present for periods of four weeks to over forty

years, it being understood that the longer periods included previous remissions. The treatment with the glycerite of hydrogen peroxide solution was necessary for periods which varied from four to thirty-eight days, 17 patients presenting complete remissions within fourteen days.

The 3 patients who showed no improvement used the solution for thirty, forty-five and seventy-five days respectively. The cultures of the first patient (Mr. C.P.), described later, presented a growth of yeast cells. The second patient (E.E.L.), presented sclerotic bilateral mastoiditis by roentgenologic examination, and the third (A.F.) had had a squamous cell carcinoma six months previously, with radical surgical treatment followed by radium therapy.

Of the patients who required penicillin in addition to glycerite of hydrogen peroxide, 2 received penicillin locally twice daily. Two others were hospitalized for treatment with penicillin. The first (F.V.A.) had been treated with glycerite of hydrogen peroxide for fourteen days and the second (W.S.) for ten days.

In order that the results may be fully evaluated, all the protocols are listed, being classified in order. The patients in whom the treatment failed are listed first, those who required combined treatment next and then, in sequence in terms of the duration of their condition, the remaining patients.

The following notes, common to all the protocols, are, for the sake of brevity, listed separately. Each of the patients suffered from chronic purulent otitis media. Treatment was initiated on the date on which cultures were taken. Each patient limited his treatment to ½ dropperful of the antiseptic solution, using it at intervals of four hours from arising until retiring. Each patient was seen on several occasions, and cultures were taken at each visit but all progress notes regarding cultural changes have purposely been omitted. In all cases the odor, when present, was either eliminated or otherwise reduced to the point at which it was no longer offensive.

PROTOCOLS OF CASES

CASE 1.—M. L., aged 45, had had otitis media in the right ear since childhood. The discharge was thick, fetid and purulent. The ear drum was absent. Culture of material taken on March 12, 1945 revealed gram-positive cocci and gram-negative bacilli. The patient used the antiseptic solution for three days, with no change in condition, and did not return for further treatment.

CASE 2.—G. E. W., aged 45, had had otitis media in the right ear for a duration of several years. The discharge was thick, purulent and fetid. The ear drum presented a large central perforation. Culture of material on Feb. 12, 1945 revealed Staph. aureus and Esch. coli. Examination on February 23 showed that the ear was about dry. The patient failed to return for further treatment or observation.

CASE 3.—C. P., aged 32, had had otitis media in the left ear for a duration of two years. The discharge was profuse and fetid. The ear drum was absent. Culture of material on Feb. 9, 1945 revealed yeast cells and gram-positive micrococci. The patient used antiseptic solution from February 9 until March 8, with little if any change in condition.

CASE 4.—E. E. L., aged 35, had chronic purulent otitis media in both ears. The duration of the disease in the left ear had been twenty years and in the right ear ten years. The condition in the right ear was now quiescent. The discharge was thick, fetid and purulent. A large polyp filled the aural canal. The ear drum was absent. Polypectomy was performed on Nov. 27, 1944. Culture of material on Feb. 17, 1945 revealed Staph. albus and nonhemolytic streptococci. The condition remained unchanged until March 19. Roentgenologic studies on March 19 demonstrated a sclerotic bilateral mastoid. There was no change in culture or condition after forty-five days of local treatment.

CASE 5.—W. S., aged 65, had had otitis media for a duration of one year. The discharge was mucopurulent. The ear drum was inflamed, with an anterior-inferior perforation. Culture of material on April 24, 1945 revealed Esch. coli and hemolytic streptococci. On May 4 the ear became painful, the mastoid tender and the discharge serosanguineous. The patient was hospitalized, and penicillin (600,000 units) was given. The condition abated, and the ear became dry in six days.

CASE 6.—F. V. A., aged 48, had had otitis media in the left ear since childhood. The discharge was thick, fetid and mucopurulent and was pooled at the tympanic end of the eustachian tube. The ear drum was absent. Culture of material on Feb. 1, 1945 revealed Staph. albus. After fourteen days there was less odor and less drainage. The patient was hospitalized on May 21 and was given penicillin (650,000 units) intramuscularly and locally every three hours. There was complete remission in five days.

CASE 7.—A. F., aged 49, on Aug. 22, 1944 presented a small papillary growth in the canal of the left ear. Biopsy performed on September 22 revealed squamous cell carcinoma. At operation on September 15 the membranous canal and tympanum were removed. Radium, 960 milligram hours, was administered on October 23. Drainage was continuous. Culture of material on Feb. 15, 1945 revealed Staph. albus and nonhemolytic streptococci. Treatment was initiated, with no improvement. On March 2 the patient was given penicillin locally, with no improvement, and on April 30 a sequestrum was removed. The condition of the patient remained unchanged. On June 5 penicillin (640,000 units) was given during hospitalization. On June 30 there had been no improvement.

CASE 8.—J. H. S., aged 37, had had otitis media on the right side for a duration of eight years. At operation in 1942, radical mastoidectomy was performed. The patient was treated for two years, without success. There was no treatment for one year. Culture of material taken on Jan. 26, 1945 revealed Staph. albus. The patient gradually improved. On March 16 there was little discharge. The patient was given local treatment with both penicillin and the new antiseptic solution. At examination on April 9, the ear was dry.

CASE 9.—S. F. H., aged 3, had had otitis media in the left ear for a duration of four weeks. The discharge was thick, fetid and purulent. Culture of material taken on May 15, 1945 revealed staphylococci, streptococci and Esch. coli. At examination on May 26, the ear was dry. The period of treatment lasted eleven days.

CASE 10.—M. L., aged 21, had had otitis media in the right ear for a duration of two months. The discharge was thick, purulent and fetid. The ear drum was perforated. Culture of material taken on April 10, 1945 revealed staphylococci, Esch. coli and diphtheroids. At examination on May 1, the ear was dry. The period of treatment lasted twenty-one days.

CASE 11.—J. E., aged 5, had had otitis media for a duration of three months. The discharge was thick, purulent and fetid. Culture of material taken April 18, 1945 revealed Staph. aureus and gram-negative bacilli. At examination on May 8, the ear was dry. At operation on June 5, tonsillectomy and adenoidectomy were done. The ear was still dry. The period of treatment was twenty days.

CASE 12.—J. F., aged 3, had had otitis media in the left ear for a duration of six months. The discharge was thick and purulent. The ear drum had a central perforation. Culture of material taken on May 4, 1945 revealed Staph. aureus. At examination on May 16, the ear was dry. At operation on June 1, tonsillectomy and adenoidectomy were performed. The ear was still dry. The period of treatment lasted twelve days.

CASE 13.—C. W., aged 30, had had otitis media for a duration of six months. The discharge was mucopurulent. The ear drum was perforated. Culture of material taken on April 12, 1945 revealed Staph. aureus and hemolytic streptococci. At examination on May 7, the ear was dry. The period of treatment lasted twenty-five days.

CASE 14.—J. F. B., aged 40, had had otitis media in the left ear for a duration of ten months. The discharge was thick, fetid and profuse. There was a large marginal perforation of the ear drum. Culture of material on May 15, 1945 revealed gram-negative bacilli. At examination on May 23, the ear was dry. The period of treatment lasted eight days.

CASE 15.—K. E., aged 10, had otitis media in the left ear. The discharge was thick, purulent and fetid. The ear drum had a large perforation. Culture of material taken on April 3, 1945 revealed staphylococci and diphtheroids. At examination on April 30, the ear was dry. The period of treatment lasted twenty-seven days.

CASE 16.—J. J., aged 7, had had recurrent attacks of acute purulent otitis media in the right ear for three years. The duration of the present exacerbation was two weeks. The discharge was thick, mucopurulent and odorless. In the ear drum, there was a perforation of the posterior-inferior quadrant. Culture of material taken on Feb. 16, 1945 revealed Staph. albus and diphtheroids. At examination on February 24, the ear was dry. The period of treatment lasted eight days.

CASE 17.—J. H., aged 38, had had chronic purulent otitis media in the left ear for a duration of three years. The discharge was thick, purulent and fetid. There was a median perforation of the ear drum. Culture of material on April 18, 1945 revealed Staph. aureus. At examination on April 23, the ear was dry. The period of treatment lasted five days.

CASE 18.—M. G., aged 19, had had otitis media in the right ear for a duration of three years. The discharge was profuse, purulent and fetid. There was a large perforation of the ear drum. Culture of material taken on Feb. 15, 1945 revealed Staph. albus. At examination on February 24, the ear was dry. The period of treatment lasted nine days.

CASE 19.—R. E., aged 27, had had otitis media in the right ear for several years. The discharge was profuse, purulent and fetid. The ear drum was

absent. Culture of material taken on Feb. 19, 1945 revealed Staph. albus and B. proteus. At examination on March 2, the ear was dry. The period of treatment lasted thirteen days. The patient returned on May 7 with a recurrent lesion, the cultures of which demonstrated an infection with Staph. albus, which cleared on May 14, after seven days of treatment.

CASE 20.—M. M. R., aged 28, had had otitis media in the right ear for a duration of five years. The discharge was mucopurulent. The ear drum was perforated. Culture of material taken on April 9, 1945 revealed staphylococci and nonhemolytic streptococci. At examination on May 2, the ear was dry. The period of treatment lasted twenty-three days.

CASE 21.—B. R., aged 28, had had otitis media in the right ear for a duration of six years. The discharge was thick, purulent and fetid and was associated with a large amount of debris. Culture of material taken on April 17, 1945 revealed Aspergillus albicans and gram-negative bacilli. At examination on May 7, the ear was dry. The period of treatment lasted twenty days.

CASE 22.—L. S., aged 30, had had otitis media for a duration of seven years. The discharge was thick, purulent and fetid. The ear drum had a central perforation. Culture of material taken on Feb. 20, 1945 revealed Staph. albus and B. proteus. At examination on March 9, the ear was dry. The period of treatment lasted nineteen days.

CASE 23.—J. F., aged 20, had had otitis media in the left ear for a duration of seven years. The discharge was thick and purulent. The ear drum had a central perforation. Culture of material taken on April 3, 1945 revealed Esch. coli, B. proteus and staphylococci. At examination on April 18, the ear was dry. The period of treatment lasted fifteen days.

CASE 24.—R. B., aged 25, had had otitis media in the right ear for a duration of ten years. The discharge had been thick and purulent continuously since mastoidectomy ten months before. A large aural polyp was present. Polypectomy was performed. Culture of material taken on Feb. 12, 1945 revealed Staph. albus and diphtheroids. At examination on February 20, the ear was dry. The period of treatment lasted eight days.

CASE 25.—W. H., aged 32, had had otitis media for a duration of ten years. He had had severe pain for two weeks. The discharge was thick and purulent, with much debris. The ear drum was large and had a marginal perforation with a cholesteatomatous mass. At operation on Nov. 16, 1944, radical mastoidectomy was performed. The discharge persisted following the surgical intervention and was resistant to all methods of treatment. Culture of material taken on Feb. 12, 1945 revealed Staph. albus. At examination on February 19 the ear was dry. The period of treatment lasted seven days.

CASE 26.—E. M., aged 27, had had otitis media in the right ear for a duration of twelve years. The discharge was profuse, fetid and mucopurulent. The ear drum had a large marginal perforation. Treatment was instituted from Nov. 21, 1944 to Feb. 9, 1945, with cleansing and administration of drops of sodium sulfathiazole solution (10 per cent), with slight improvement. Culture of material taken on February 9 revealed hemolytic staphylococci and gram-positive micrococci. At examination on February 20, the ear was dry. The period of treatment lasted eleven days.

CASE 27.—M. G., aged 32, had had otitis media in the right ear for a duration of twelve years. The discharge was thick and fetid. The ear drum had a large

perforation. Culture of material taken April 25, 1945 revealed Esch. coli. At examination on May 5, the ear was dry. The period of treatment lasted ten days.

CASE 28.—A. B., aged 21, had had bilateral otitis media since childhood. The discharge from both ears was thick and purulent. Both ear drums were absent. Culture of material taken on April 24, 1945 revealed Staph. aureus and Esch. coli. Examination on May 4 showed that the ears were dry. The period of treatment lasted ten days.

CASE 29.—M. W., aged 25, had had otitis media in the right ear since childhood. The discharge was thick and purulent. The ear drum had an anterior-inferior perforation. Culture of material taken Feb. 12, 1945 revealed Staph. albus and diphtheroids. At examination on February 19, the ear was dry. The period of treatment lasted seven days.

CASE 30.—H. L., aged 25, had had otitis media in the right ear since childhood. At examination on Aug. 24, 1943, a large aural polyp was found and there was a thick, purulent discharge. At operation on Dec. 2, 1945, radical mastoidectomy was performed. There were exacerbations and remissions of aural discharge from Feb. 19, 1944 until Feb. 16, 1945. The present exacerbation has lasted three months. Culture of material taken Feb. 16, 1945 showed Staph. albus and diphtheroids. At examination on March 2, the ear was dry. The period of treatment lasted fourteen days.

CASE 31.—E. S., aged 28, had had otitis media in the right ear since childhood. The discharge was mucopurulent. The ear drum had a small perforation in the anterior-inferior quadrant. Culture of material taken April 30, 1945 revealed Esch. coli. Examination on May 3 showed that the ear was dry. The period of treatment lasted four days.

CASE 32.—G. S., aged 30, had had otitis media in the left ear for a duration of twenty years. At operation on Nov. 2, 1944 radical mastoidectomy was performed. The discharge was purulent and resistant. Treatment instituted from Nov. 20, 1944 until Feb. 1, 1945 consisted in aural cleansing and dressing every three days. Ear drops, boric acid, sulfathiazole solution (5 per cent), hydrogen peroxide and alcohol were administered. Culture of material taken Feb. 1, 1945 revealed Staph. aureus. Examination on February 22 showed that the ear was dry. The period of treatment lasted twenty-one days.

CASE 33.—R. H., aged 34, had had recurrent otitis media since childhood. The discharge was tenacious and mucopurulent. The ear drum had a large anterior-central perforation. Culture of material taken on June 25, 1945 revealed Staph. albus. At examination on June 30, the ear was dry. The period of treatment lasted five days.

CASE 34.—A. E. S., aged 35 had had otitis media in the right ear since childhood. At operation on Jan. 25, 1945, polypectomy was performed. The discharge was thick and purulent. Treatment instituted from January 25 to February 5 consisted in administration of sulfathiazole drops. The condition of the patient remained unchanged. Culture of material taken on February 12 revealed Staph. albus. At examination on March 2, the ear was dry. The period of treatment lasted twenty-five days.

CASE 35.—H. R., aged 35, had had otitis media for a duration of thirty years. The discharge was thick and fetid. The ear drum had a large central perforation. Culture of material taken on Feb. 13, 1945 showed staphylococci, streptococci and

B. proteus. At examination on March 11, the ear was dry. The period of treatment lasted twenty-six days.

CASE 36.—F. E. H., aged 52 had had otitis media in the left ear for a duration of thirty years. The present exacerbation had lasted three weeks. The discharge was profuse and fetid. The ear drum was absent. The membrane of the middle ear was swollen. Culture of material taken on Feb. 5, 1945 revealed Staph. albus and hemolytic streptococci. At examination on March 15 the ear was dry. The period of treatment lasted thirty-eight days.

CASE 37.—G. H., aged 54, had had recurrent otitis media since childhood. The present exacerbation had lasted several months. The discharge was fetid and purulent. The ear drum was large, with a central perforation. Culture of material taken April 9, 1945 revealed gram-negative bacilli and micrococci. At examination on April 18, the ear was dry. The period of treatment lasted nine days.

SUMMARY

Thirty-seven patients suffering from chronic purulent otitis media due to mixed bacterial infections and resistant to the usual forms of treatment were given topical applications of a new antiseptic solution consisting of hydrogen peroxide (1.5 per cent) derived from urea peroxide (4 per cent) in glycerin. Of these patients, 2 failed to return, 3 showed no improvement and 3 required additional treatment. Two patients experienced vertigo. In no patient was there evidence of local irritation.

In 29 patients, the condition cleared completely in periods varying from four to thirty-eight days. Seventeen of the patients presented dry ears within fourteen days.

It is suggested that hydrogen peroxide (1.5 per cent) derived from urea peroxide (4 per cent) in glycerin has a beneficial effect in the treatment of chronic purulent otitis media.

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ATRESIA OF THE EXTERNAL AUDITORY CANAL OCCURRING IN MILITARY SERVICE

A Report on the Correction of This Condition in Ten Cases

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THE WAR with its associated violence presented the otorhinolaryngologist with many new entities and unique problems. One of these entities, which is relatively uncommon in civilian practice but not too rare in military service, is atresia of the external auditory canal secondary to gunshot wound. The steel helmet only partially protects the ear even under ideal conditions. In the confusion of battle this protection is further diminished by angulation or loss of the helmet in maneuvering over obstacles. In general, the ear receives considerable protection from descending missiles, but objects of force traveling from any side angle or upward may seriously injure the ear. This type of injury usually includes one or more of the organs adjacent to the area of the ear.

The anatomic structure of the external auditory canal responds poorly to this type of trauma and places a handicap on the surgeon. The external canal is approximately 1½ inches (about 4 cm.) in depth and is composed of an outer cartilaginous portion and an inner bony portion, the two of about equal length. Its average diameter is about ⅜ inch (9.5 mm.) with the vertical usually exceeding the horizontal diameter. The direction of the canal is inward and forward, with somewhat of a dome at about its midportion. The cartilaginous section of the tube is lined with skin and subcutaneous tissue containing sebaceous and ceruminous glands and hair follicles. The inner or bony part of the tube is characterized by absence of these glands, and the skin is rather snugly attached to the periosteum. The two portions of the tube are connected by fibrous bands. Movement of the mandible in the temporomandibular joint on mastication is transmitted actively to the anterior membranous canal wall. Around these immediate structures lie the mastoid process, the middle ear, the dura and the brain, the seventh and eighth cranial nerves, the temporomandibular joint and the mandible, and the deep structures of the upper part of the neck. Many of these anatomic features are of critical importance in the evaluation of atresia and its correction.

The 10 cases analyzed in this report illustrate various types and degrees of atresia secondary to gunshot wounds and other traumas.

These cases are divided into four groups depending on the types of atresia: (1) web type, (2) solid fibrous healed type, (3) solid fibrous and bony healed type and (4) infected fibrous and bony type.

All the subjects were combat soldiers with an average age of 26 years. None had had a previous history of aural disease. Eight were

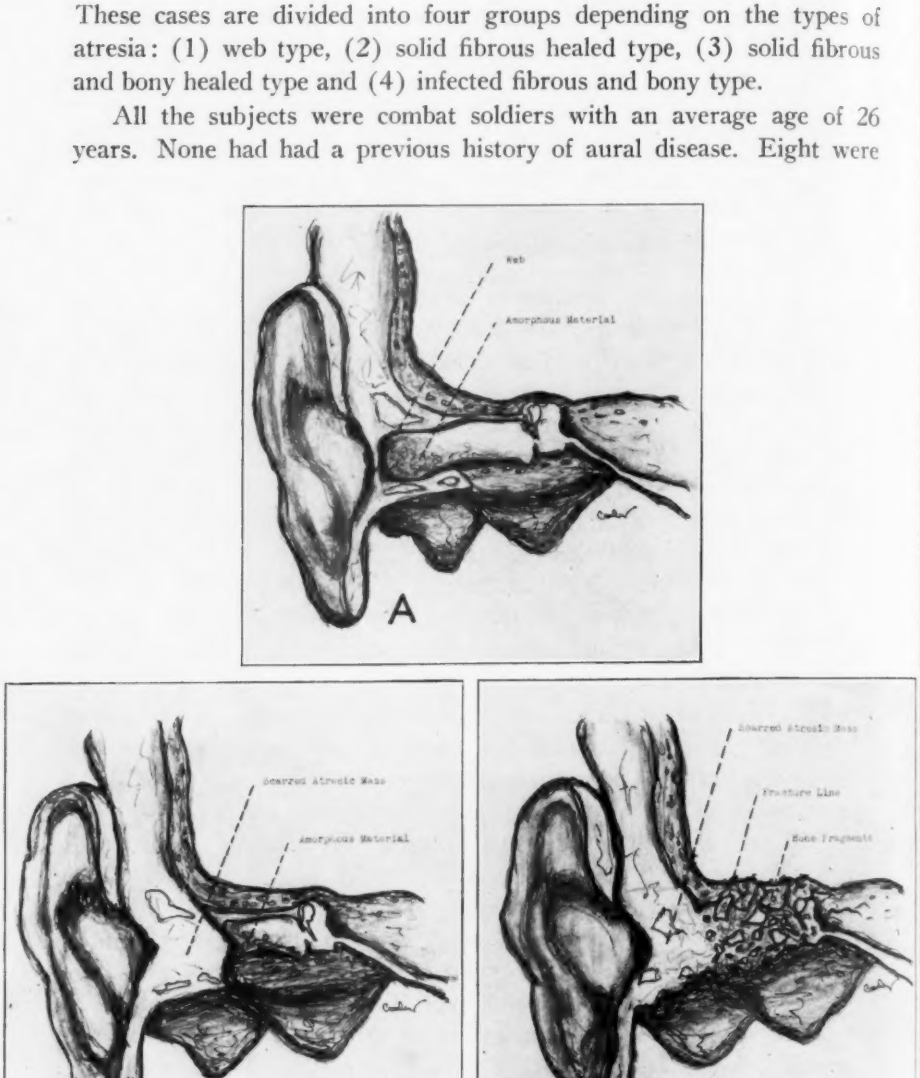

Fig. 1.—Types of atresia: *A*, web type; *B*, solid fibrous healed type; *C*, solid fibrous and bony healed type.

injured in battle by sharpnel or mortar or machine gun fire, 1 sustained a fractured skull in falling from a truck and another in an airplane accident. The points of entrance of the missiles varied from the immediate area of the ear to the middle and posterior portions of the neck and from a point posterior to the pinna to one anteriorly

located, in the region of the cheek. In 4 patients there was mild to moderate deformity of the pinna. Eight patients were standing and 2 were prone when injured. Right and left ears were involved in equal numbers. Atresia was complete in all but the 2 infected canals, where fistulas, granulation tissue and pus were present in the scarred mass.

OBSERVATIONS ACCORDING TO TYPES

1. *Web Type* (fig. 1A).—There are 2 cases in this group. Each patient received a simple, localized wound about the membranous portion of the external auditory canal. Scarring was minimal. A roentgenogram of the area showed no fracture. Neurologic examination indicated normality. There was air conduction deafness, and

Fig. 2.—Ear after atresia of the web type had been corrected.

nerve conduction was moderately diminished. The pinna was normal, and the patient was essentially asymptomatic except for moderate tinnitus. When a needle was inserted into the stenotic area, a lack of resistance was encountered after the web had been penetrated.

Corrective measures in the simple, uncomplicated type of case are accomplished by excising the web and adjacent scar tissue through the endaural approach and implanting a thin, split, free skin graft over the denuded areas. It may be necessary to remove a small portion of conchal cartilage to facilitate the creation of the new opening (fig. 2). All normal skin in the area is saved for the repair. Alteration of bone is not indicated in this type of procedure. The graft should be stablized by being carefully stitched to the external skin margins. The

uninvolved portion of the bony canal is loosely packed with gauze, and, on top of this, tiny fragments (1 by 2 mm.) of a cut-up foam rubber sponge are packed over the graft to secure it (fig. 3). The rubber fragments may be impregnated with a sulfonamide compound or penicillin, and it is wise to administer one of these compounds systemically also. Mastication should be reduced to a minimum during the healing period to put the graft at rest. This is accomplished by providing a liquid and soft diet or a nasal feeding tube.

The operative findings in addition to that of the atretic web were interesting. There was a moderate collection of moist whitish amorphous material resembling cholesteatoma. In both cases the tympanic mem-

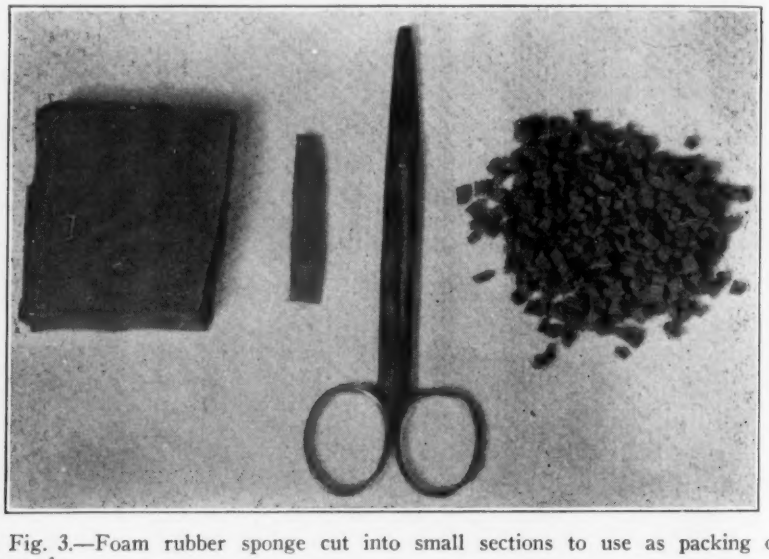

Fig. 3.—Foam rubber sponge cut into small sections to use as packing on the graft.

brane was perforated centrally. There was no evidence of infection in the middle ear. The time elapsing since the injury was six weeks in one case and eight weeks in the other and the corresponding post-operative periods of healing were eighteen and twenty-one days. As there is a tendency toward contracture of a hollow tube in soft tissue following skin grafting, the original correction was slightly exaggerated. Hearing tests of air and bone conduction showed no improvement.

2. *Solid Fibrous Healed Type* (fig. 1B).—The 3 cases of this group were similar in many respects to those of the foregoing group. The difference was principally one of degree of injury and repair. In 1 case the pinna was scarred slightly. The wounds were deeper. The hearing responses, the roentgenograms, the results of neurologic exami-

nation and the subjective reactions were about the same as those previously described. However, the needle test showed prolonged resistance to insertion.

This type offered a few more difficulties in correction. A prehelix, preconchal incision down to the periosteum was required to remove the mass of scar tissue. Salvage of all available skin was essential to the creation of flaps to minimize the loss of skin and to facilitate healing. Frequently the periosteum was destroyed by the trauma, but great care was exercised to preserve as much of it as possible. When the newly created meatus was not ample, the skin and periosteum were reflected inward, the tunnel was enlarged by removing some of the bone on the inferior, posterior and superior walls of the canal and then the tissue was replaced on its new bed. Again the raw surfaces were covered carefully by a thin, split graft, which was maintained in position by packing with sponge rubber fragments. Prophylactic measures favoring healing were undertaken.

Operation revealed a more extensive amount of scar and a smaller quantity of the soft, whitish cholesteatomatous material beyond it. One drum membrane presented a moderate-sized central perforation. The other two were perforated in Shrapnell's area, and the perforations were covered with a portion of the split graft. Strangely, the grafts remained over the perforations and appeared to be viable. This statement is made with reservation because the grafts placed over the small perforations may not live; they may be simply stretched and glued to the area as a small piece of parchment would be and eventually may separate. In the interim the perforations appear to be eliminated. The periods intervening between the injuries and their correction were eight, six and nine weeks, and the postoperative healing periods were twenty-nine, thirty and twenty-four days. Hearing was not improved.

3. *Solid Fibrous and Bony Healed Type* (fig. 1 C).—In this group there was the added factor of fractured bones. These bones may be present as detached bony fragments, crushed and compressed but not markedly displaced, or there may be a series of linear fracture lines. The ones which were shattered were the most difficult to deal with.

Diagnostic features were more striking than in the previous two groups. The wounds were deeper, with more scarring, and there was considerably more damage to the surrounding structures. Roentgen examination usually showed fracture of the mastoid process. Two patients had in addition concomitant fractures of the mandible, the maxilla and other parts of the skull. Only 1 retained moderate bone conduction. The pinna was altered in 2 patients, and tinnitus was marked. Headaches were common. At the time of my investigation,

neurologic findings were not significant, but there was evidence that previously vertigo, nystagmus and weakness of the facial nerve had existed in varying degrees after the injury. The needle test was not indicated.

Operation in this type was tedious. Radical mastoidectomy was frequently necessary, and it was always required to carry out some type of bone work. An endaural incision proved ideal, and the separation required great care and patience because of the increased possibility that important structures of the area might be surgically injured (fig. 4). The dura, the bulb of the jugular vein, the sigmoid sinus and the facial nerve were of special interest. The normal surgical landmarks had been markedly distorted, especially about the middle ear.

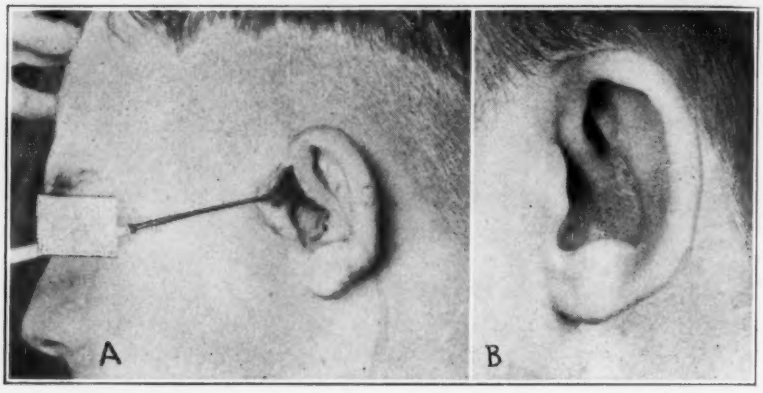

Fig. 4.—*A*, appearance of ear on the seventh postoperative day, with packing out; *B*, same ear healed six weeks later.

Two of the 3 patients were treated by endaural radical mastoidectomy. There were disconnected bony fragments in the mass of atretic scar tissue. In these 2 the middle ear was compressed and fractured in several directions. There were fracture lines extending through the labyrinth and cochlea. A secondary thin split skin graft was performed after a healthy bed of granulations tissue covered the site, four weeks after operation. The facial nerve was exposed in 1 of the 2 patients, but no weakness followed. Both had dead labyrinths and dead cochleas (fig. 5). In the third patient mastoidectomy was not performed, although some of the mastoidal air cells were exposed in eliminating the atretic mass. The drum membrane had been perforated centrally, but there was no infection. The labyrinth reacted to stimulation. A primary skin graft was implanted. On the second postoperative day, frank lobar pneumonia developed, and the patient was treated with 100,000 units of penicillin daily for five days. The

convalescence from the pneumonia was uneventful. However, the dressing of the ear presented a foul odor on the fifth postoperative day. All packing was removed on the sixth postoperative day because of a secondary infection in the wound. Very little of the graft survived, and an infection of the middle ear was now present. If the therapy for the suppuration of the middle ear is successful a secondary grafting of skin will be attempted at the previously stenotic area. If the middle ear cannot be cleared up, radical mastoidectomy is indicated. There

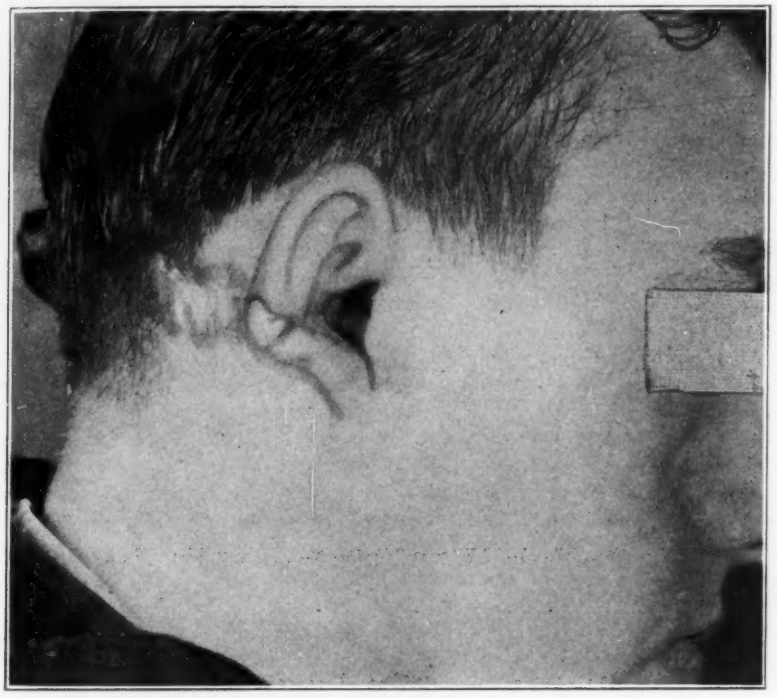

Fig. 5—Postoperative result of correction of atresia. Note the evidence of concomitant injury to the cheek, the maxilla, the facial nerve, the parotid gland, the mandible, the pinna and the region of the mastoid process.

was little evidence to suggest the presence of cholesteatomatous material in any of these cases. It is likely that in this type of case a longer period must intervene between injury and treatment if this phenomenon is to develop. The intervening periods were eight, twelve and eleven weeks. The periods of healing were six and seven weeks in the first 2 cases. In the third case it is as yet undetermined.

4. *Infected Fibrous and Bony Type.*—The 2 cases in this group were essentially the same as those in the preceding group plus the presence of a suppurating process. Suppuration in this area under

these circumstances is an extremely dangerous situation. The roentgen and neurologic findings, the results of the hearing tests and the subjective complaints were significant. Suppuration was manifested either by a moderate amount of purulent material discharged through one or more fistulous tracts, and granulation tissue, or by a low grade infection localized about a sequestrum with little obvious discharge. The former proved more serious. The needle test was not advisible.

Procrastination in the treatment of patients with this type of atresia may be disastrous, and it is here that chemotherapy and biotherapy used prophylactically against an intracranial complication are most helpful. In almost all cases radical mastoidectomy is indicated.

One of the patients in this group sustained a severe fracture of the temporal bone by falling from a truck onto the side of his head. The ear discharged blood and cerebrospinal fluid. Complete facial paralysis developed immediately and there was a severe labyrinthine reaction, which gradually subsided over a three month period. There was no improvement in the responses of the facial nerve after six months. Atresia was complete except for a small posterior fistulous tract that drained pus. An endaural radical mastoidectomy was performed. The middle ear had been crushed, and there were several fractures in the mastoid process. One line of fracture ran through the promontory, the fallopian canal and the labyrinthine capsule. There was some displacement of the fragments, but they were solid and well fixed. No attempt was made to remove them. The facial nerve was exposed surgically in the middle ear and the mastoid areas, and it was seen to be torn at the angle above the descending portion. The ends were prepared and sutured carefully with two fine tantalum wire sutures after the nerve had been displaced into the middle ear cavity and advanced anteriorly. Because of the previous presence of a low grade infection in the area, it was anticipated that a secondary repair would eventually be necessary. As the cavity "granulated in" postoperatively, faradic testing revealed the reaction of regeneration. A secondary skin graft was subsequently placed in the cavity, and the patient gradually recovered approximately 50 per cent function. Regretfully I observed that the ear did not become completely dry; there was persistent draining from a small area located anteriorly in the region of the tube. Both the labyrinth and the cochlea were dead. The time intervening was seven months (fig. 6).

The other patient in this group had atresia of the external auditory canal secondary to a gunshot wound. There was considerably more scarring than in the previous case. A fragment of bone containing the facial nerve was manipulated during the radical mastoidectomy, and paresis lasting one month resulted. Secondary skin grafting was performed. The time intervening was three months and the postoperative healing time three months. The labyrinth and cochlea of this patient were also dead.

Until the advent of the war, atresia of the external auditory meatus resulting from wounds about the ear was strikingly uncommon. In atresia secondary to tumor growth, the therapy of the tumor is of first importance. Atresia resulting from burns and infections of the external canal, however, may be handled similarly to the first two

groups discussed here. I have no experience in attempting to dilate atretic structures with molds. It would appear that in a case of mild partial atresia of the web type the aperture could be dilated successfully. It is doubtful if dilatation would be of any real value in the treatment of any of the other types of atresia.

Considerable reason exists for the treatment of this condition. Surgical correction affords an estimation of the status of the ear and presents specific knowledge rather than conjecture. In great measure

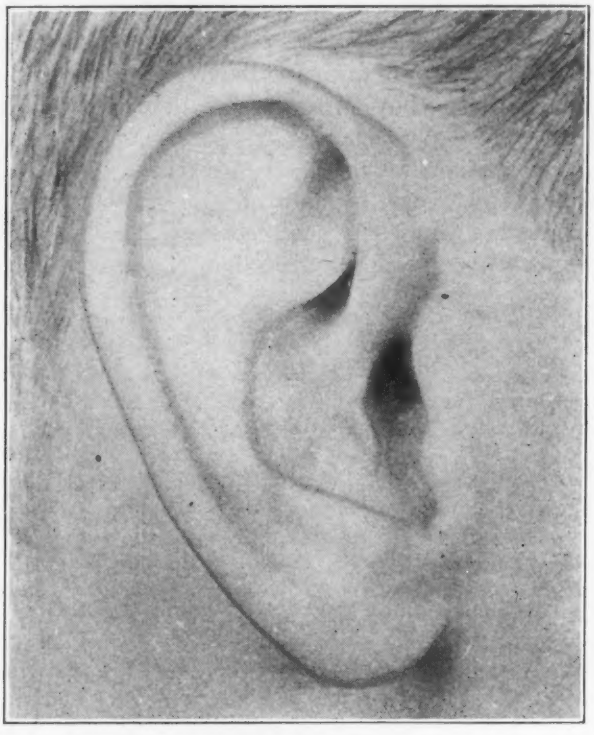

Fig. 6.—Postoperative result of correction of atresia.

it eliminates the possibility of internal and external secondary cholesteatoma. It eradicates concealed or apparent secondary infection in this area. One of the important aspects is the prophylaxis obtained against intracranial complications in the last group by eliminating the focus of infection and a certain number of the pathways.

I am not familiar with the incidence of prevention of atresia of the types described. However, it would appear that the first two especially could be prevented by the use of a mold or a pack in the canal and early skin grafting. There is considerable gratification in the fact that the vast majority of patients injured in this way have

received either penicillin or a sulfonamide derivative and that frequently the injured parts have healed before the patients reach the zone of the interior.

SUMMARY AND CONCLUSIONS

Atresia of the external auditory canal is not uncommon in the military service.

Ten cases were classified into four groups requiring individual attention.

The endaural surgical approach is ideal.

Application of a primary, thin, split, free skin graft after excision of the scar causing the atresia is the treatment of choice for simple fibrous atresia. A technic of implanting the free graft has been described.

When the adjacent bony structures are destroyed, radical mastoidectomy is frequently advisable.

When there is suppuration in the presence of shattered adjacent bones, radical mastoidectomy is indicated.

Prophylactic biotherapy and chemotherapy are helpful, especially in the group with fractures and suppuration.

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EFFECT OF ZEPHIRAN CHLORIDE, TYROTHRICIN, PENICILLIN AND STREPTOMYCIN ON CILIARY ACTION

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AND
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THIS study was made to determine what effect, if any, solutions of zephiran chloride, tyrothricin, penicillin and streptomycin have on the ciliary activity of the mucous membranes of the upper respiratory tract.

MATERIALS AND METHODS

The Animal Used.—Twenty normal healthy rabbits were used for the entire study. Five were utilized for each of the four drugs in question.

Preparation of the Mucous Membranes.—The ciliated mucous membranes were studied by two methods. In one they were extirpated and placed in the solutions in question. In the other they were left intact and bathed with the solutions that were being tested.

For removal of the ciliated mucosa the animal was given a lethal dose of either pentobarbital sodium or ethyl carbamate U.S.P. (urethane) intravenously. A midline incision of the skin of the nose was made, following the bridge throughout its entire length. The periosteum was elevated and the bones covering the nasal chamber, but not that immediately overlying the septum, were removed with a chisel. Care was taken not to perforate the underlying nasal mucosa. The exposed membrane was then cut away with a small scissors and immediately placed in saline solution (0.9 per cent). The septum was next removed in toto with as little trauma as possible to the septal mucosa. This was accomplished by placing the blades of a small scissors flat against the floors of the nasal fossae with the septum between the blades. Then the septum was freed from its attachment to the palate by cutting along its base in a posterior direction. The bridge of the nose immediately between the eyes was cut in a vertical direction until the floor of the nasal chamber was reached. In this manner the two incisions met at right angles to each other at the posterior border of the septum. Thus the septum was freed from all of its attachments except the bridge of the nose. This bony bridge was next grasped by a forceps and the entire structure removed and placed in a Petri dish containing 0.9 per cent saline solution. In order to remove the septal mucosa the bony bridge was held securely with a large tissue forceps. A small, curved forceps was slipped around the mucous membrane at its posterior free edge. With this the mucosa was elevated and removed by pulling it *slowly* toward the anterior tip of the septum.

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This was done first on one side of the septum and then on the other. In this way the septal ciliated mucosa was removed with as little trauma as possible.

In the case of the experiments with streptomycin the mucous lining of the trachea was studied as well. In each of the 5 rabbits the trachea was exposed. It was then removed in toto and placed in 0.9 per cent saline solution. For study it was split longitudinally and divided into several small squares. The tracheal mucous membranes were studied microscopically for the presence of active cilia before they were placed in the solutions in question. This was done by putting sections of the membranes on a plain clean microscopic slide, which was placed on the stage of a microscope. A direct beam of light was focused on the sections from above. A magnification of 160 was used. The membranes were kept moist by applying a drop or two of saline solution periodically. This was very necessary, for once the membrane became even slightly dry, the cilia ceased beating. Those sections bearing active cilia were placed in the solutions in question.

In the study with penicillin the second method, in which the mucosa was left intact, was used in 2 cases. The animal was anesthetized with ethyl carbamate, administered intra-abdominally. The procedure then followed the same pattern until the mucosa underlying the nasal bones was reached. Instead of the mucosa being removed, it was split and folded back. The solution in question was applied continuously for the time prescribed. The two membranes were then removed and studied microscopically for moving cilia.

It should be emphasized that the membranes were never allowed to become dry. While they were being studied microscopically, they were kept moist with the solution being tested.

Solutions Used.—The zephiran chloride was supplied by R. A. Jarecki, of the Winthrop Chemical Company, New York. Both aqueous and saline solutions of the concentrations 1:1,000 and 1:2,000 were used. Controls with plain distilled water and isotonic solution of sodium chloride were set up for each case studied.

The tyrothricin proved to be insoluble in distilled water and was precipitated by the mineral salts in the saline solution. Consequently, it was employed as a suspension in distilled water. A concentration of 1:5,000 has been recommended for topical application by Crowe and co-workers.[1] In this study concentrations of 1:2,000 and 1:5,000 were used. Distilled water served as the control in each case.

Penicillin was dissolved in isotonic solution of sodium chloride. Concentrations of 200 units per cubic centimeter and 500 units per cubic centimeter were used. It has been recommended by the National Research Council[2] that for topical application 200 to 250 units per cubic centimeter of solution should be employed. Isotonic solution of sodium chloride was used as the control in these studies.

Streptomycin was also made up in isotonic solution of sodium chloride. It was used in concentrations of 100 units, 300 units, 500 units and 1,000 units per cubic centimeter, respectively. The control solution was isotonic solution of sodium chloride.

We should like to emphasize that for each solution and for each animal studied a control solution was also used, the type depending on the solvent in question.

1. Crowe, S. J.; Fisher, A. M.; Ward, A. T., Jr., and Foley, M. K.: Ann. Otol., Rhin. & Laryng. **52**:541-573, 1943.

2. Keefer, C. S., and others: Penicillin in the Treatment of Infections. J. A. M. A. **122**:1217-1224 (Aug. 28) 1943.

Time Element.—Proetz [3a] estimated that "the entire nasal blanket (mucous) is discarded into the pharynx at the rate of at least once every half hour." If this is true, then it would not be likely that a solution topically applied would remain in the nasal chambers for any great length of time, provided that the cilia were active. Therefore, two hours was the time limit in most of the studies if the cilia were active that long. In the case of zephiran chloride the experiments were conducted for one hour. In 4 of the experiments with streptomycin the membranes were studied also at the end of twenty hours.

RESULTS

Zephiran Chloride.—Aqueous solutions of zephiran chloride with concentrations of 1:1,000 and 1:2,000 stopped all ciliary activity of extirpated ciliated mucous membranes in five to ten minutes. The membranes appeared as if they had been fixed. The controls, which were treated with plain distilled water, showed cessation of ciliary action in five to ten minutes as well.

However, zephiran chloride (1:1,000 and 1:2,000) in isotonic solution of sodium chloride had no apparent deleterious effect on the active cilia. In both the experimental and the control solutions the cilia were beating actively at the end of one hour.

Comment: The deleterious effect of distilled water on ciliary action has been previously reported by Proetz.[3a] Proetz [3] also noted that 0.9 per cent saline solution was not toxic to active cilia.

Tyrothricin.—Actively beating cilia treated with *aqueous suspensions* of tyrothricin in concentrations of 1:2,000 and 1:5,000 stopped beating in five to ten minutes. This was also true of the controls treated with plain distilled water.

Comment: No evidence was obtained as to whether or not the tyrothricin, of itself, was toxic to the actively beating cilia, since it could not be suspended or dissolved in 0.9 per cent saline solution.

Penicillin.—In this study 5 animals were also used, but 2 of them were merely anesthetized with ethyl carbamate, administered intraabdominally. The ciliated mucosa was exposed surgically and allowed to remain intact. In this way the blood supply was retained.

In one of the animals whose nasal membranes were exposed surgically, 200 units of penicillin per cubic centimeter of isotonic solution of sodium chloride was applied continuously for two hours on one side of the septum. On the other side, isotonic solution of sodium chloride was applied alone. The cilia when studied microscopically appeared undis-

3. Proetz, A.: (*a*) Essays on the Applied Physiology of the Nose, St. Louis Annals Publishing Company, 1941; (*b*) Ann. Otol., Rhin. & Laryng. **54**:94-95, 1945.

turbed and were beating actively on both sides of the septum at the end of the two hour period.

In the other animal penicillin was used in the concentration of 500 units per cubic centimeter of 0.9 per cent saline solution. This was applied continuously to the mucosa on one side of the septum, while isotonic solution of sodium chloride was administered to the opposite side. No deleterious effect on the activity of the cilia was noted. The cilia treated with this concentration of penicillin in 0.9 per cent saline solution were beating just as actively as were those treated with the control solution. From the 3 remaining animals the ciliated mucous membranes were removed and placed in penicillin concentrated to 200 units and 500 units per cubic centimeter of 0.9 per cent saline solution. Three controls, 1 for each animal, were established with isotonic solution of sodium chloride. There was no marked retardation of ciliary action in any of these. At the end of the two hour period the cilia treated with penicillin dissolved in 0.9 per cent saline solution were beating just as actively as were those treated with isotonic solution of sodium chloride alone.

Comment: Similar findings have been reported by Lierle and Evers [4] and Proetz.[3b]

Streptomycin.—Streptomycin in concentration of 100 units, 300 units, 500 units and 1,000 units per cubic centimeter of isotonic solution of sodium chloride had no apparent deleterious effect on ciliary action of the mucous membranes at the end of two hours. There was no apparent difference between these and the 5 controls treated with isotonic solution of sodium chloride. In the experiments with streptomycin tracheal ciliated respiratory epithelium was used alongside the mucosa from the nasal chambers. There occurred no apparent difference. The cilia of the tracheal mucosa were beating just as vigorously at the end of two hours as were those of the nasal mucosa. In 4 cases it was possible to examine the membranes twenty hours after their initial immersion in the differently concentrated solutions of streptomycin. Although the ciliary activity had become slower than it was during the first two hours, it compared favorably with that of the controls left in isotonic solution of sodium chloride.

Comment: Proetz [3b] has stated that the respiratory epithelium of the trachea may be used for such studies as well as the epithelium from the nose. Our evidence has further substantiated this claim.

COMMENT

Should Aqueous Solutions Be Used to Irrigate the Nasal Chambers?—Proetz [3a] has already shown that distilled water inhibited ciliary activ-

4. Lierle, D. M., and Evers, L. B.: Laryngoscope **54**:176-185, 1944.

ity of the nasal mucosa in his experiments. This was confirmed repeatedly in our experiments when distilled water was used either as a control or as a solvent for the substance in question. Thus the aqueous solutions of zephiran chloride (1 : 1,000 and 1 : 2,000) and tyrothricin (1 : 2,000 and 1 : 5,000) proved to be toxic to the cilia. All of the cilia thus treated stopped beating in five to ten minutes. Perhaps if physiologically isotonic concentrations of these substances could have been used, this toxic effect of hypotonicity might have been eliminated.

Was the Value of Isotonic Solution of Sodium Chloride Lessened by the Addition of the Substances in Question?—For as long as our experiments were conducted (usually two hours, but one hour in the experiments with zephiran chloride, and twenty hours in 4 of the experiments with streptomycin) the value of 0.9 per cent saline solution was not noticeably lessened when zephiran chloride (1 : 1,000 and 1 : 2,000), penicillin (200 units and 500 units per cubic centimeter) and streptomycin (100 units, 300 units, 500 units and 1,000 units per cubic centimeter) were added to it. The membranes treated with the solutions in question bore cilia which, so far as we could determine, appeared to be beating as rapidly and as strongly as those treated with isotonic solution of sodium chloride alone.

It should be remembered that these experiments were all done on ciliated mucosa taken from normal healthy rabbits. The results reported here should be compared with those of studies made on extirpated human ciliated nasal mucosa. This would have two advantages: (1) It is the human nose in which we are most interested and human material would give us a better clue as to how it would behave under such treatment, and (2) the mucosa from a human subject is usually removed because it is diseased, and since these solutions are indicated in such cases, their effects would be much better evaluated were they so studied.

CONCLUSIONS

1. Aqueous solutions of zephiran chloride (1 : 1,000 and 1 : 2,000) and tyrothricin (1 : 2,000 and 1 : 5,000) were deleterious to the ciliary activity of the nasal mucosa of normal healthy rabbits.

2. Plain distilled water stopped all ciliary activity of such membranes when it was applied.

3. Isotonic solution of sodium chloride proved not to have any appreciable deleterious effect on the ciliary action of nasal mucosa and of tracheal mucosa taken from normal healthy rabbits.

4. Zephiran chloride (1 : 1,000 and 1 : 2,000) in isotonic solution of sodium chloride had no inhibitory effect on the ciliary action of the nasal mucosa of healthy rabbits.

5. Penicillin in concentrations of 200 units and 500 units per cubic centimeter of isotonic solution of sodium chloride had no apparent deleterious effect on the ciliary action of the nasal mucosa taken from normal healthy rabbits.

6. Streptomycin in concentrations of 100 units, 300 units, 500 units and 1,000 units per cubic centimeter of isotonic solution of sodium chloride had no inhibitory or deleterious effect on the ciliary action of either nasal mucosa or tracheal ciliated epithelium of normal healthy rabbits.

Case Reports

REMOVAL OF A TORTILLA FROM THE ESOPHAGUS

D. BERNSTEIN, M.D., BROOKLYN

A TORTILLA is "a thin flat unleavened cake, as of maize, baked on a heated iron or stone."[1] This flat dough is rolled about a center of spiced ground meat. The preparation is a fairly common article of diet in the southwest region of the United States. That it could cause esophageal obstruction is almost incredible. A case in which a tortilla caused complete occlusion of the lumen of the esophagus is therefore reported.

REPORT OF A CASE

A 47 year old white man was admitted to the Tucson, Ariz., Veterans' Administration Facility at 3 p. m., Oct. 15, 1942. He complained of inability to swallow and of dyspnea. He was rather emotionally unstable, and the history was not easy to elicit. Twenty minutes prior to admission, while eating a tortilla, he felt some of it "stick" in his throat. Thereafter he was unable to swallow anything, even water. He complained also of a dull pain localized to an area in the midline of the neck just above the sternum. There was no history of any similar episode.

He had previously been admitted to a Tucson hospital, July 31, 1942, for "acute lumbago of the right flank." His military, family and past history were not contributory. He was a fairly well developed and nourished white man. The lungs were clear. The heart was not enlarged. The blood pressure was 130 systolic and 90 diastolic; the pulse rate, 88; the sinus rhythm, regular. There was no sclerosis of the peripheral vessels. His abdomen was soft and nontender throughout. Neurologic examination showed deep tendon reflexes to be equal and active. There were no pathologic reflexes. Mentally the patient was, as previously mentioned, inclined to instability. On both his admissions to the hospital it was noted that he was too sick to give a complete history. Nevertheless, a thorough investigation of the patient's complaint was decided on.

The urine had a specific gravity of 1.012. Its color was amber and its reaction acid. It contained no albumin and no sugar. The sputum revealed no tubercle bacilli.

A blood complement fixation test for syphilis and a precipitation test made at the previous admission were negative.

Fluoroscopy, as anticipated, showed no evidence of foreign body. A no. 1 capsule filled with barium sulfate was given to the patient to swallow. It descended no farther than the level of the second dorsal vertebra. This was confirmed by roentgenogram.

Esophagoscopy was done at 3:45 p. m. the day of admission. The laryngopharynx was anesthetized by means of a 2 per cent tetracaine hydrochloride

From the Veterans Administration Facility, Tucson, Ariz.

1. Webster's New International Dictionary, ed. 2, Springfield, Mass., G. & C. Merriam Company, 1942.

spray. An 8 mm. esophagoscope was passed without difficulty to a point just below the cricopharyngeus muscle, to the upper third of the esophagus. A translucent doughy grayish mass was there visualized completely occluding the esophageal lumen. I had had a fair personal acquaintance with the composition of the tortilla and realized that the usual biting and grasping forceps would be of no avail. The dough would swell when in a moist medium and become rather firmly glued to the walls of the viscus. The esophagoscope was simply passed farther and the mass circumscribed in its lumen. Whatever remained adherent to the walls of the esophagus was disregarded. The doughy mass could be seen to enter the lumen of the esophagoscope until it obscured the light completely. It became firmly attached to the metallic walls of the instrument and was promptly removed by withdrawing the esophagoscope. On removal it was observed to be a firm round doughy mass 15 mm. in length and 8 mm. in width.

The patient expressed a sensation of immediate relief, sat up on the table and swallowed a glass of water. He was discharged the next day and has been symptom free to date.

COMMENT

As expressed by Vinson,[2] "The esophagus is particularly intolerant to the presence of a foreign body." Except in rare instances,[3] an inflammatory reaction and possibly fatal mediastinitis will quickly result. Any patient with the slightest suspicion of an esophageal foreign body should therefore be given the promptest attention.

The use of a capsule containing barium sulfate rather than liquid barium sulfate was preferred in order to avoid possible coating of the foreign body with the thick white liquid and making its visualization and removal more difficult. The use of a capsule is also of advantage when partial obstruction is suspected inasmuch as the capsule will lodge directly at the occluded area.

Finally it should be noted that this patient was discharged the next morning and promptly returned to work. Esophagoscopy when accomplished with a minimum of local anesthesia and a minimum of trauma should produce no greater period of disability.

1342 Fifty-First Street.

2. Vinson, P. P.: Foreign Bodies in the Air and Food Passages, M. Clin. North America **16**:1471, 1933.

3. Weaver, D. F.: Presence of a Chicken Bone in the Esophagus for Fifty-Six Days, Arch. Otolaryng. **38**:60 (July) 1943.

Progress in Otolaryngology

Summaries of the Bibliographic Material Available in the Field of Otolaryngology

ADVANCES IN THE UNDERSTANDING OF RHINOLOGIC AND OTOLOGIC CONDITIONS RELATED TO THE NERVOUS SYSTEM

A Critical Survey of the Literature

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(Continued from page 541)

AURAL AND NASAL CONDITIONS IN HYPOPHYSIAL DISEASES

Deafness in Hypophysial Cachexia (Simmonds' Disease[178]).

In the case of tuberculoma of the anterior lobe of the hypophysis reported by Kirschbaum and Levy,[179] the patient, a man aged 44, had deafness (with associated eunuchoidism and blindness). He also had severe dizzy spells with increasing difficulty in walking for three years and had been completely bedridden for two years. Both hearing and vision had begun to fail thirty years before his admission to the hospital, and for the past eight years he had been totally deaf and blind.

Examination.—His skin was smooth, dry and yellowish. Examination of the eyes revealed clouding of the lens and scleral irregularities. The musculature was generally flaccid. A dextrose tolerance test showed a fasting blood sugar level of 60 mg. per hundred cubic centimeters. After 100 Gm. of dextrose had been administered orally, the blood sugar levels, determined at hourly intervals, were 107, 120, 140 and 148 mg. per hundred cubic centimeters of venous blood. The patient died from what was thought to be terminal bronchopneumonia.

Diagnosis Made at Necropsy.—Four conditions were noted: 1. Sclerosed tuberculoma of the anterior lobe of the pituitary gland. The anterior lobe was completely replaced by dense connective tissue with scanty, deeply stained nuclei. In places the connective tissue was infiltrated with small round cells of lymphocytic type and single larger histiocytes. The posterior lobe of the hypophysis was intact. 2. Female distribution of body hair. 3. Atrophy of the adrenal cortex. 4. Fibrocaseous tuberculous primary complex in the lower lobe of the right lung.

178. Simmonds' disease (Morris Simmonds, Hamburg physician, 1855-1925). Hypophysial cachexia includes a triad of symptoms—premature aging, rapid atrophy of the genital organs with repression of the secondary sexual characters, and loss of hair, noted usually in comparatively young women, due to atrophy or diminished functioning of the hypophysis cerebri.

179. Kirschbaum, J. D., and Levy, H. A.: Tuberculoma of the Hypophysis with Insufficiency of Anterior Lobe: A Clinical and Pathologic Study of Two Cases, Arch. Int. Med. **68**:1095-1104 (Dec.) 1941.

Authors' Comment.—Neighborhood meningitis or osteomyelitis of the sphenoid bone may be associated with tuberculoma of the hypophysis. Early miliary generalized tuberculosis (according to Ranke's classification) may have been present.

Compression of the seventh nerve may give rise to manifestations.

Pituitary cachexia, or Simmonds' disease, due to a destructive lesion of the glandular parenchyma of the anterior lobe is rarely caused by tuberculosis.

Comment (W. P. E.).—It seems that the deafness in this case of Simmonds' disease may have been due to failure of the normal metabolic changes, produced by pressure or by disease of the anterior lobe of the pituitary gland in early life. It is in early life that the internal secretions are most necessary for the development and functioning of the cells of Corti, which are involved in deficiency disease.

Craniopharyngioma (Erdheim's Tumor) as a Cause of Simmonds' Disease.

Simmonds' disease following destruction of the pituitary gland by a craniopharyngioma may appear fairly early in life, this tumor being congenital in nature. In 2 instances Farber and associates [180] found that the craniopharyngioma arose from embryonic rests of the original pituitary duct or stalk—the craniopharyngeal portion of the hypophysis. Cystic degeneration had occurred, and the capsule of the tumor was infiltrated with bone.

In the case reported the findings included retardation of growth, polydipsia and polyuria, mental retardation, hypotension, impairment of vision and ocular disturbances, dryness of skin, pathologic sleep, depression of basal metabolism with hypopyrexia, and absence of secondary sex characteristics, shown in atrophic breasts and genitalia as well as in lack of axillary and pubic hair. This rather varied clinical picture certainly suggests a polyglandular syndrome with evidence that the gonadotropic, thyrotropic, adrenotropic and growth-promoting hormones of the pituitary gland were diminished or absent.

The Four Hypophysial Syndromes Offering Surgical Possibilities.

Only four hypophysial syndromes offer surgical possibilities: (*a*) Fröhlich's adiposogenitalism with its chromophobe adenoma, (*b*) acromegaly with its eosinophilic adenoma, (*c*) Cushing's disease with its basophilic adenoma, and certain cases of (*d*) Simmonds' disease with its hypophysial atrophy.[181]

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180. Farber, J. E.; Goldstein, K., and Beswick, W. F.: Simmonds' Disease: Simmonds' Disease with a Cranio-Pharyngioma, J. Clin. Endocrinol. **1**:688-690 (Aug.) 1941.

181. Rossier, J.: Hypophysis and Surgery, Schweiz. med. Wchnschr. **72**:380-395 (April 4) 1942; abstracted, Reese, H. H.; Lewis, N. D. C., and Sevringhaus, E. L.: The 1942 Year Book Neurology, Psychiatry and Endocrinology, Chicago, The Year Book Publishers, Inc., 1942.

Intranasal Surgical Approach to Pituitary Tumors.

Nager [182] dedicated his Semon Lecture of 1939, "The Paranasal Approach to Intrasellar Tumors," to Harvey Cushing who wrote, in his "Consecratio Medici," ". . . There is only one thing that can effectively bind people and that is a common devotion."

Chiari in 1911 described his transethmoidal and transsphenoidal approach to intrasellar tumors. Hager states: *"By using Chiari's modification of the extracranial exposure of the sella we get a short rather large funnel-like access to the sellar region with a good survey and without danger to the surrounding parts."*

The chief indications for the paranasal route are a large intrasellar tumor with special forms of visual troubles, viz., central scotoma and homonymous hemianopsia. On the other hand, a tumor with suprasellar extension is better reached by the transfrontal method.

Nager [183] states: "It seems, therefore, that if Chiari's modification is used, Cushing's recommendation of the transsphenoidal methods in 1912 is even to-day of value."

There was no immediate postoperative mortality among all the 13 patients on whom Nager performed seventeen operations for intrasellar tumors by Chiari's method. Seven of the 13 patients are still alive. Three died from adenocarcinoma at intervals of one month to a year. One patient succumbed from accidental bronchopneumonia seven years after the operation. One patient died from hemorrhage of the nose after having worked intensively for three years. "The autopsy showed an erosion of the internal carotid on the roof of the sella probably due to a late necrosis in consequence of the application of radium after the operation."

For patients with hydrocephalus this operation has proved very dangerous, the postoperative mortality being three fifths.

Technic.—The operation is performed under local anesthesia, injections being directed alongside the inner wall of the orbit to reach the ethmoid nerve. Then the lateral nasal wall is followed submucously "to the sphenoethmoidal region. . . . All the ethmoid cells are removed . . . so that in the depth . . . the anterior wall of the sphenoid sinus is visible. By its resection the posterior wall becomes exposed, especially if also the intersphenoidal septum and the rostrum including the end of the nasal septum are removed."

TUMOR OF THE BRAIN

Causes and Locations of Central Disturbances Producing Nystagmus in Patients with Tumors of the Brain.

Nylén [184] regards head-positional nystagmus as a particularly important sign of a tumor in the posterior fossa (Güttich,[185] 1934; Howe, 1938).

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182. Nager, F. R.: The Paranasal Approach to Intrasellar Tumors: Semon Lecture, 1939, J. Laryng. & Otol. **55**:361-381 (Aug.) 1940.

183. Nager, F. R.: L'opération des tumeurs intrasellaires par la voie transethmoidale de Chiari, in Extrait des comptes-rendus du Congrès des Médecins alienistes et neurologistes, 1936; cited by Nager.[182]

(Footnotes continued on next page)

The most recent researches indicated its relatively frequent occurrence with cerebral tumors in supratentorial localizations (Mygind; Moberg; Seiferth). With tumor of the posterior fossa the spontaneous nystagmus is nearly always of the combined type, horizontal, rotatory and vertical nystagmus. It is easily influenced by "only lateral or side position" or by "several positions."

With tumor of the anterior or the middle fossa the nystagmus is, on the contrary, most frequently vertical downward and appears most often "only in hanging head position."

The local changes from the tumor must exert an influence through the position of the head as such, which itself acts as the releasing factor.

On account of the extreme pressure—or changes in the circulation which appear in a low position of the head—the tumor either directly or indirectly disconnects centers or tracts which are connected with the normal balance of the eyes in the sagittal plane, no matter whether the pressure takes place near the tumor, at a small distance from it or through contrecoup action (on the corpora quadrigemina region or the vermis).

Explanation of Nystagmus in Patients with Tumors of the Brain.

Vertical nystagmus could be explained by pressure near the incisura (notch) cerebelli [186] when the tumor is in the region around the aqueductus sylvii. Pressure on the tracts of the cerebrum may take place when the tracts pass the incisura cerebelli, in which case a condition similar to "decerebrate rigidity" with increased reflex activity—amongst others a vertical nystagmus—appears as a result.[184] This agrees with Bailey's explanation of the tonic cervical reflexes occurring in certain patients with pinealoma.

Clovis Vincent discovered the temporal compression, "the tightening" of the most medial region of the temporal lobe toward the edge of the tentorium, whereby the isthmus cerebri is deformed.

Behrman [187] showed that a vertical nystagmus downward occurs just in this hanging position of the head in normal persons with caloric irritation in one ear, independent of the temperature of the water.

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184. Nylén, C. O.: The Oto-Neurological Diagnosis of Tumours of the Brain, Acta oto-laryng., 1939, supp. 33, pp. 1-151.

185. Güttich, A.: Otologische Erfahrungen bei der Untersuchung von Hirntumoren, Ztschr. f. Hals-, Nasen- u. Ohrenh. **36**:78-164, 1934.

186. Incisura cerebelli anterior B N A (semilunar notch), a wide shallow notch on the anterior surface of the cerebellum occupied by the brachia conjunctiva and the inferior quadrigeminal bodies. Stedman, T. L., and Garber, S. T.: Stedman's Practical Medical Dictionary, ed. 15, Baltimore, William Wood & Company, 1942, p. 544.

187. Behrman, W.: Observations concernant la détermination des positions indifférantes, antérieures et postérieures, dans le nystagmus calorique après un lavage unilatéral, Acta oto-laryng. **21**:346-350, 1934.

"Mesencephalic Deafness" Associated with Tumor of the Brain.—Brunner [188] stated that an interruption of the auditory fibers between the inferior colliculus of the corpora quadrigemina and the medial geniculate body (acoustic isthmus) produced so-called mesencephalic deafness in cases of glioma invading the corpora quadrigemina and the corpus pineale. Mesencephalic deafness is usually a late symptom of tumor of the pineal body. It is commonly accompanied by hyperirritability of the labyrinth. In these cases secondary cochlear atrophy plays a role similar to that which it plays in deafness caused by tumor of the eighth nerve. A pinealoma penetrating into the third ventricle will impair auditory conduction sooner than a tumor of the quadrigeminal plate which penetrates the pulvinar.

Glioma in Corpora Quadrigemina and Corpus Pineale (Nylén [189]).

Bailey (1936) pointed out as the cause of deafness "the pressure" against the medial geniculate body, and Glaser, "the pressure" against the lateral lemniscus. However, it is doubtful whether one can attach any especial value to Siebenmann's [190] hearing scheme—concentrically unilateral or bilateral reduction with shortened bone conduction—as typical for glioma in these regions. Nylén thinks that this hearing syndrome has too many resemblances to those which the tumor can cause wherever it has its localization.

Complete Mesencephalic Deafness from a Midbrain Tumor Infiltrating the Tegmen (Sloane, Persky and Saltzman).[191]

The outstanding feature was sudden and complete deafness in a man with a glioma infiltrating the tegmentum of the midbrain who had previously shown moderate impairment of hearing.

Also present were (*a*) neighborhood throat symptoms due to extension of the tumor, as well as (*b*) the hypothalamic symptoms of hypersomnolence and (*c*) mental changes.

The patient, aged 55, was admitted to the hospital with a history of impairment of hearing of eighteen months' duration. At the outset he complained of weakness and pain in the legs. There had been increasing loss of sexual potency. He had been under treatment for impaired hearing; catheterization of the eustachian tubes had afforded some relief.

One week before admission an audiometric examination showed a hearing loss of 40 to 60 decibels at the higher tone levels; the impairment in the lower tone

188. Brunner, H.: Zur Klinik der Mittelhirnaubheit, Monatschr. f. Ohrenh. **69**:1049-1061 (Sept.) 1935; abstracted, Eagleton, W. P.: Eagleton's Index and Abstracts of Literature on Progress in Intracranial Lesions Related to Aural and Nasal Conditions, Newark, N. J., 1941, reprint (1937), p. 32.

189. Nylén,[184] p. 104.

190. Siebenmann: Ueber die zentrale Hörbahn, Ztschr. f. Ohrenh. **29**:28, 1896.

191. Sloane, P.; Persky, A., and Saltzman, M.: Midbrain Deafness: Tumor of the Midbrain Producing Sudden and Complete Deafness, Arch. Neurol. & Psychiat. **49**:237-243 (Feb.) 1943.

range was but 20 to 30 decibels. This suggested that the neutral mechanism of hearing was at fault, the deafness not being of the conduction type.

The patient had been able to carry on his occupation until about two weeks prior to admission to the hospital, although his wife stated that he slept most of the time and that it was difficult to arouse him. Sudden complete deafness and nystagmoid movements of his eyes led to hospitalization.

Examination.—Ears: Tuning forks showed the hearing lost to both high and low notes and bilateral absence of bone conduction; the audiometer, complete loss of hearing in both ears. Eyes: There were a few nystagmoid jerks on movement of the eyes in all directions. The pupils reacted sluggishly to light but better to accommodation. Throat: The gag reflex was absent bilaterally, and there was drooping of the soft palate on the right side. Both knee jerks were absent.

The spinal fluid was under a pressure of 130 mm. of water.

Course of Illness.—Within a week the patient became stuporous and incontinent. It was difficult to arouse him, but when he finally awakened, he seemed to be alert and cooperative.

A few days later his responses became irrelevant. Weakness of the right arm developed, and the deep reflexes in this limb were increased.

Death occurred seventeen days after admission. The patient showed terminal coma, with pulmonary edema.

Autopsy.—A neoplasm in the brain stem extended from the posterior part of the hypothalamus, infiltrating the midbrain and the pons. It involved the entire tegmentum of the midbrain and the pons, particularly on the left side. The tail of the tumor, projecting between the cerebellar hemispheres, hollowed out a shallow indentation in both hemispheres and compressed the dorsal aspect of the medulla. (The aqueduct of Sylvius, while displaced toward the right side, was not blocked.)

The hypothalamus contained a fairly large tumor mass.

Microscopic Diagnosis.—The diagnosis was mixed glioma, essentially astrocytoma or astroblastoma.

The authors state: "The association of fixed pupils and absence of knee jerks suggested syphilis of the central nervous system (tabes), but the results of serologic studies were negative."

Comment (W. P. E.): Anatomic Reason Why Tumors of the Brain Stem Cause Deafness.—Impairment of hearing may result from a tumor involving the trapezoid bodies in the pons, as the trapezoid fibers leaving the ventral cochlear nucleus become the specific fibers on the ventrolateral surface of the rostral extreme of the medulla oblongata, above which the trapezoid fibers ascend in the pons until they become buried midway between the surface and the fourth ventricle.

Authors' Comment.—In a study of 15 patients with pontile tumor Horrax found unilateral deafness present in 4 and questionable impairment of hearing in 1.

Brunner in 1936 stated that tumors of the tegmentum of the midbrain are likely to give rise to sudden and complete deafness.

Brunner summarized the causes of "mesencephalic deafness" as (1) a tumor of the mesencephalic tegmentum of the crus cerebri which develops caudally from the red nucleus (the tegmental nucleus), (2) any thalamomesencephalic tumor, (3) a pineal tumor or (4) a suprasellar tumor.

A Case of Deafness from a Pontile Tumor.—In Throckmorton's [192] case (1926) the earliest symptom was a "queer feeling" in the head, a feeling as if the patient at times would fall, associated with a mental state such that, should the equilibrium be actually lost, no will power would be in reserve to prevent a fall from taking place. Later, change of posture would at times produce a feeling of dizziness, and not infrequently it was necessary for the patient to "collect himself" following postural change before he felt certain that he could maintain his equilibrium while sitting or walking.

For a number of years he had been aware of some loss of hearing in the right ear, but not until the loss in the left ear became almost total was much consideration given to these losses of hearing.

Examination.—Hearing was greatly reduced in both ears, ticks being heard only when a watch was placed in contact with the left ear and within 1 inch (2.5 cm.) of the right ear. Air conduction was better than bone. The Galton whistle tests showed hearing for 4, 5, 6½ and 8 absent on the right side, and the high tone limit reduced to 6 on the left side.

While the soft palate was drawn somewhat to the left side, the tip of the tongue protruded in the median line.

Horizontal nystagmus was present: coarse movements to the left, fine movements to the right. Associated with the horizontal nystagmus was a well pronounced vertical nystagmus, pointing to the possibility of a left-sided lesion.

The Bárány tests did not produce nausea.

Ventriculograms revealed nothing significant.

Aside from the nystagmus, the palsy of the sixth nerve and the loss of hearing in the left ear, the evidence seemed mostly in favor of a left frontomotor lesion.

There was progressive diminution of hearing in the left ear until the hearing disappeared.

Necropsy.—A hemorrhagic glioma of the left half of the pons varolii was found. The resulting hemorrhage in the pons, interfering with fibers or nucleus, caused the palsy of the sixth nerve.

Dr. George A. Moleen, of Denver, said that nystagmus and especially the nerve deafness on that side were suggestive of a lesion of the brain stem, particularly of the anterior superior quadrant of the pons.

Dr. Throckmorton stated that there was no question as to the involvement of the brain stem, evidenced by the fact that the man had *gradually diminishing hearing on the left side associated with a weakness of the sixth nerve.* The first symptom that he presented was some disturbance in the equilibratory apparatus, with nystagmus, both horizontal and vertical.

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192. Throckmorton, T. B.: Glioma of Pons Varolii Simulating a Frontomotor Tumor, Tr. Sect. Nerv. & Ment. Dis., A. M. A., 1926, pp. 187-196; J. A. M. A. **87**:1731-1735 (Nov. 20) 1926.

The vertical nystagmus, the progressive diminution of hearing in the left ear, the weakness of the left external rectus muscle, and the motor weakness of the right lower part of the face and of the right arm and the right leg can all be readily explained by a left-sided pontile lesion.

Cranial Chordoma Causing Deafness.

Chordoma of the basiocciput and basisphenoid has its growth largely within the cranial cavity. In one fifth of the cases it appears in the nasopharynx.

Eighty-five cases of cranial chordoma have been reported, to which Boldrey and McNally [193] add 4.

CASE 1.—A man aged 26 complained that his hearing and vision were failing. When examined he was almost completely blind and deaf. The involvement of the brain included the second, fifth, sixth, seventh, ninth, tenth and twelfth cranial nerves. Roentgenograms showed erosion of the clinoid processes and of the sella turcica. At autopsy a whitish pink, opaque, cheesy tumor covered the basiocciput and the basisphenoid.

CASE 2.—A man aged 21 had deep occipital pain on the left side, vertigo, fine lateral nystagmus, and a heavy feeling in the upper part of the left side of the jaw. There was slight edema of the left optic nerve. Autopsy disclosed a yellowish rubbery nodular tumor at the junction of the basiocciput and the basisphenoid. A thin plate of bone separated the tumor from the mucous membrane of the sphenoid sinus.

CASE 3.—A woman aged 50 complained of severe headache, tinnitus in both ears and double vision. The involvement of the brain included the right third, seventh, eighth and twelfth cranial nerves. A roentgenogram showed destruction of the basiocciput, the basisphenoid and the right petrous apex. The mass in the epipharynx was firm and tough.

CASE 4.—A girl aged 16 had transitory weakness of the right lateral rectus muscle four years before admission. There was recurrence two years before admission, with gradual loss of hearing and vision. Examination showed complete loss of function of the second, fourth, sixth, seventh and eighth cranial nerves bilaterally. The third, eighth, ninth, tenth, eleventh and twelfth nerves appeared to be partially involved. Roentgenograms showed tumor of the sella turcica with erosion of both petrous pyramids. A mass could be seen in the nasopharynx.

Authors' Comment.—Chordoma grows so slowly that even in the absence of treatment many years elapse before death. Radium and roentgen therapy undoubtedly were of benefit in case 3.

A hypophysial chordoma was reported by Goerke [194] in 1931.

193. Boldrey, E., and McNally, W. J.: Chordoma of the Basiocciput and Basisphenoid, Arch. Otolaryng. **33**:391-394 (March) 1941; abstracted, Arch. Neurol. & Psychiat. **47**:850-851 (May) 1942.

194. Goerke, M.: Zur Pathogenese und Klinik der traumatischen Innenohrschädigungen, Ztschr. f. Laryng., Rhin. **20**:363-374 (March) 1931.

A Primary Epithelioma of the Maxillary Antrum Which Caused "Garcin's Syndrome" Without Signs of a Metastatic Nasopharyngeal Tumor Until Fourteen Months Later.

In 1927 Garcin [195] described his syndrome in connection with the diagnosis of tumor of the nasopharynx involving the base of the skull. He emphasized three symptoms:

(1) Unilateral involvement of all the cranial nerves.

(2) Early absence of motor or sensory or other symptoms of involvement of the brain.

(3) Early absence of signs of increased intracranial pressure, namely, of papilledema or of increased pressure of cerebrospinal fluid as evidenced during lumbar punctures.

In Spiegel's [196] case during a period of over three years there was nothing to suggest a nasopharyngeal tumor except haziness of the right maxillary sinus.

The patient, aged 56, had two teeth of the right side of the upper jaw extracted two years previously. Two months later numbness developed over the right side of the upper lip and within one year involved the entire right side of the face. At the same time there was loss of taste over the right side of the tongue and the right side of the oral cavity. Later complete ptosis of the right eyelid appeared with progressive bulging of the eyeball. Six weeks previously the hearing in the right ear diminished. During these six weeks the patient became completely blind in the right eye and unable to move the eye.

The patient was hospitalized at the Brooklyn Jewish Hospital Dec. 10, 1940. Neurologic examination showed proptosis of the right eye, pallor of both optic disks, and paralysis of the third, fourth, fifth, sixth, seventh and eighth nerves, with weakness of the twelfth nerve, on the right side. The left knee jerk was overactive; the left plantar reflex, diminished.

Roentgenograms of the skull suggested a tumor in the right half of the base of the skull. Laminography revealed a defect in the right cribriform plate and a blurring of the structure of the orbit and the right anterior clinoid process, suggesting a destructive lesion.

Craniotomy disclosed a grayish tumor on the right side in the anterior and middle fossae. It was hard, elastic and adherent to the base of the skull. *The pathologic report was metastatic carcinoma.*

Fourteen months later, Jan. 26, 1942, the patient was admitted to the Montefiori Hospital.

Neurologic examination showed all the cranial nerves on the right side involved except the seventh. An Oppenheim sign was elicited on the left.

A roentgenogram showed some irregularity of the body of the twelfth vertebra suggestive of metastatic involvement. Roentgenograms of the paranasal sinuses

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195. Garcin, R.: Le syndrome paralytique unilatéral global des nerfs crâniens, Thesis, Paris, A. Legrand, 1927.

196. Spiegel, L. A.: Syndrome of Garcin—Unilateral Total Involvement of the Cranial Nerves with Report of One Case, Ann. Otol., Rhin. & Laryng. **52**: 706-712 (Sept.) 1943.

revealed a haziness of the outline of the internal wall of the right antrum and slight haziness of the left frontal sinus.

Death occurred June 10.

Necropsy.—The brain showed a sheetlike mass of tumor extending from the anterior to the posterior fossa. Though the tumor was predominantly on the right side some of it had crossed the midline. In addition there were isolated nodules attached to the inner surface of the dura. All the cranial nerves on the right side were atrophied. There was marked destruction of the sella turcica. No pituitary body was seen.

Metastases were present in the liver, the adrenal glands, the pleurae and the vertebrae.

Microscopic Examination of Tumor.—The tumor consisted of highly variable columns of cells, widely separated by a vascular, edematous stroma. The columns of tumor cells contained cystlike spaces. The tumor cells were small, closely packed, with little cytoplasm and relatively small dark vesicular nuclei.

The final diagnosis was "epithelioma adenoides cysticum, probably arising in the right maxillary sinus."

From the pathologic report and the fact that an operation had been performed on the right maxillary sinus it was apparent that the tumor had secondarily invaded the base of the skull.

Complete Destruction of the Pituitary Gland by Nasopharyngeal Tumors Without Clinical Signs.

In several cases a nasopharyngeal tumor penetrating the cranial cavity has apparently destroyed the pituitary gland completely without any clinical signs of pituitary insufficiency being observed.

Needles [197] has found extensive destruction of the pituitary gland without clinical signs in cases of basal tumors having their origin in the paranasal sinuses.[198]

Other basal tumors, e.g., chordoma, affect the cranial nerves bilaterally and may give rise to signs of increased pressure, as reported by E. D. Friedman and L. Stevenson (Tumors Involving Ventral Aspect of Pons and Medulla, Including Two Chordomas, Brain **59**:291-301 [Oct.] 1936).

DIABETES AND INTRACRANIAL COMPLICATIONS OF SUPPURATIVE OTITIS

Uncontrollable Hyperglycemia and Persistent Leukocytosis as an Indication of Operation in Mucosus Otitis in a Diabetic Patient.

In Bisi's [199] opinion, diabetes does not tend to increase the hazard of Streptococcus mucosus infection, because of the use of insulin. Diabetic patients should be treated for months with large doses of sulfanil-

197. Needles, W.: Malignant Tumors of the Nasopharynx, J. Nerv. & Ment. Dis. **86**:373-398 (Oct.) 1937.

198. Spiegel also refers to an article by C. Davison and S. Kahr (Carcinoma of the Sphenoid Sinuses with Invasion of the Cranial Cavity, Arch. Otolaryng. **14**:16-22 [July] 1931).

199. Bisi, H.: Otitis a neumococus mucosus y diabetes, Rev. de otorrhinolaryng. **2**:125-127 (Dec.) 1942.

amide and sufficient insulin and given a diet to control the hyperglycemia. Furthermore, there should be adequate surgical intervention whenever hyperglycemia and leukocytosis persist; for historical studies reveal that in a diabetic patient all the cells of the temporal bone participate in the inflammatory reaction of acute otitis.

The lateral sinus should be explored for a possible thrombus even in the absence of symptoms of sinus thrombosis. General anesthesia is contraindicated.

Frequency of Postoperative Erysipelas in Pneumococcic Mastoiditis.

Druss and Allen [200] studied mastoiditis in 49 diabetic persons. In 43 per cent the infection was due to Pneumococcus type III. Destruction of bone occurred earlier than in nondiabetic patients. The high incidence of postoperative erysipelas (27 per cent) they explain by "the increase in sclerosis of the smaller vessels, which resulted in a poor blood supply for the soft tissues and bone."

Renal Insufficiency and Toxic Manifestations of Sulfathiazole Poisoning in a Diabetic Patient Suffering from Meningitis Caused by Pneumococcus Type III.

In the case reported by Myers, Robb and Clapper,[201] of meningitis caused by Pneumococcus type III in a diabetic patient, with recovery, bronchopneumonia developed during sulfathiazole therapy. There was sudden renal insufficiency with retention of sulfathiazole. The possible toxic manifestations from the sulfonamide drug were stupor, delirium and generalized epileptiform convulsions.

The patient, a woman aged 46, had diabetes mellitus, diagnosed in 1934. Three years prior to her admission to the hospital she discontinued the use of insulin and ceased to follow a diabetic diet.

Late in 1939 she experienced an acute illness with running nose, sore throat, dry cough and bilateral earache. December 26 both ear drums ruptured spontaneously. During the succeeding week she had irregular fever with chilly sensations and sweats. Hearing was greatly diminished. Jan. 4, 1940 weakness and ataxia developed in the right hand and soon extended to the right arm and leg. January 6 a clonic convulsion occurred in the right hip, which spread to the right leg, then to the right arm, lasting about a minute.

During the next five days the patient had five to ten similar attacks daily. About fifteen seconds before the onset of each attack there would be a sense of epigastric discomfort—a warning of an impending convulsion. During the attacks she was unable to speak but did not lose consciousness.

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200. Druss, J. G., and Allen, B.: Acute Mastoiditis in Diabetes Mellitus, Arch. Otolaryng. **36**:12-22 (July) 1942.

201. Myers, G. B.; Robb, J. M., and Clapper, M.: Type III Pneumococcus Meningitis, J. Michigan M. Soc. **40**:280-283 (April) 1941.

She was hospitalized January 11, complaining that her ears had been draining since December 26 and that there had been right-sided convulsions of five days' duration.

Examination.—There was a bilateral purulent discharge, with tenderness over the draining mastoid process, associated with bilateral middle ear deafness. There was also lateral nystagmus, with quick component to the left, and also slight vertical nystagmus. The left pupil was slightly larger than the right. The left optic fundus revealed a cotton wool patch and slight arterial narrowing.

The blood pressure was 180 systolic and 110 diastolic.

The neurologic findings were: distinct muscular weakness and hypotonia of the right arm and leg; biceps, triceps, patellar and ankle jerks diminished on the right; definite ataxia on the right; asynergy and dysmetria of the right arm and leg; adiadokokinesis of the right arm; no stiffness of the neck.

The convulsions were typical of the jacksonian epilepsy characteristically associated with supratentorial lesions. The neurologic examination, however, pointed to a right cerebellar rather than a cortical lesion.

Roentgenograms showed cloudiness of the right mastoid process and of the petrous portion of the temporal bone, and slight cloudiness of the left mastoid process.

Preoperative Course (January 11 to 16).—Slight elevation of temperature was noted evenings. The concentration of blood sugar was 286 per cent. The urine contained glucose. There was no significant acidosis.

The patient was restricted to a diet of 206 Gm. of glucose and given 30 units of protamine zinc insulin and 10 units of regular insulin daily. The glycosuria was reduced to a trace, but the fasting blood sugar ranged between 0.170 and 0.250 per cent. Spinal puncture (January 12) showed the spinal fluid under pressure, 125 mm. of water; the fluid contained 2 white blood cells per cubic millimeter.

Operation (January 17).—Mastoidectomy was performed on the right side. The mastoid process was filled with granulation tissue and contained pus. A small perforation of the dura led into a cyst, 2 by 5 cm., which was aspirated.

Development of Pneumococcus Type III Meningitis.—January 18 her temperature was 104 F. January 19 she was irrational, her neck was rigid and Kernig's sign was positive. Spinal puncture showed cloudy fluid with 12,100 polymorphonuclear leukocytes; no organisms were seen on smear.

Since Staphylococcus aureus had been isolated from the aural discharge, administration of sulfamethylthiazole was started on the supposition that the meningitis was also staphylococcic. In the eighteen hour interval the patient received a total of 10.5 Gm. of sulfamethylthiazole, without any demonstable effect. Spinal fluid taken two and one-half hours after the last dose contained 16,500 polymorphonuclear leukocytes per cubic millimeter and was positive for pneumococcus type III. A total of 14 Gm. of sulfathiazole was given on January 20, the first 5 Gm. intravenously (sodium salt), the remainder by mouth.

Dramatic Response of Meningitis to Sulfathiazole.—The following morning the patient was mentally clear, her temperature normal. The spinal fluid contained 472 cells per cubic millimeter and no organisms. The dosage of sulfathiazole was 2 Gm. every four hours (six times daily). The cell content of the spinal fluid dropped to 5 per cubic millimeter February 2.

Development of Bronchopneumonia During Sulfathiazole Therapy.—January 24 the patient had a chill and her temperature climbed to 104.6 F. A blood culture was positive for nonhemolytic Staph. aureus. January 25 there were roentgenographic signs of consolidation in the lower lobe of the left lung. The blood level of free sulfathiazole on the morning of consolidation was 6.7 mg. per hundred cubic centimeters. The sputum was negative for Pneumococcus.

Her temperature was 100 F. and 102 F. until January 29, when it fell to normal.

Development of Renal Insufficiency with Retention of Sulfathiazole.—The patient received 10.5 Gm. of sulfamethylthiazole on January 19 and a total of 127 Gm. of sulfathiazole by January 30. Blood concentrations of free sulfathiazole during the first week ranged from 1.2 to 8.1 mg. per hundred cubic centimeters.

Between January 19 and 28 she complained of nausea and vomited. January 29 she became drowsy and disoriented.

Coincident Nitrogen Retention.—The blood urea was 96 mg. per hundred cubic centimeters on February 2, then fell gradually to 60 mg. on February 8 and to 38 mg. on February 23. On that date, twenty-four days after the use of sulfathiazole had been discontinued, renal function was still impaired. The urea clearance rose to 87 per cent on March 13, but ability to concentrate was impaired. In spite of the absence of hematuria and urinary acetylsulfathiazole calculi, the renal insufficiency was considered a toxic manifestation of sulfathiazole poisoning. Paralleling the nitrogen retention, there was a fall in blood carbon dioxide-combining power.

Since the diabetes was well controlled, the fall in blood carbon dioxide-combining power was attributed to the renal insufficiency.

Toxic Manifestations Preferable to the Central Nervous System.—January 29 the patient became drowsy and disoriented, this change being coincident with an abrupt rise in blood sulfathiazole to 20 mg. per hundred cubic centimeters. The next morning she was delirious. January 30 generalized epileptiform convulsions developed. January 31 the blood level of the drug was 15.1 mg. per hundred cubic centimeters. "The convulsions were probably not due to hypoglycemia, because two occurred while an intravenous injection of dextrose was in progress.

"By a process of exclusion as well as by the fact that the stupor, delirium and convulsions appeared coincidentally with the abrupt rise of blood sulfathiazole and gradually disappeared as the blood level fell, it was concluded that the cerebral symptoms were probably due principally to sulfathiazole retention.

"Convulsions have been reported in animals from the intravenous injection of sodium sulfapyridine, but not from sulfathiazole. It is possible that the coexisting intracranial infection was a conditioning factor."

Comment (W. P. E.): Immediate Closure of Dura in Cases of Threatened Meningitis.—The meningitis was probably caused by the opening of the dura and the draining of the cerebellar cyst in the presence of a suppurative process in the mastoid process.

After having had several unfortunate experiences in accidentally opening the dura in cases of threatened meningitis with sterile cerebrospinal fluid, we at the Newark Eye and Ear Infirmary have learned to close the dural defect immediately with a flap of mucous membrane taken from the inside of the lip, the dura adhering at once. In larger defects we have used fascia lata.

Arteriosclerosis and Infected Thrombi from Diabetes, Meningitis and Abscess of the Brain, with Sequestration of the Labyrinth; Four Cases of Sequestration of the Labyrinth (Proctor and others [202]).

Necrosis of the petrous bone is to be expected frequently in patients with diabetes, probably as a result of the lodging of infected thrombi in the arteriosclerotic vessels found universally in patients with diabetes.

Of 4 patients with sequestration of the labyrinth, 1 died of cerebellar abscess.

SENSE OF SMELL AND OF TASTE

Physiology of Smell.

We are still extremely ignorant of the way in which sensations of smell are produced (Adrian and Ludwig [203]).

Adrian and Ludwig summarize their observations as follows: 1. The action of the olfactory organs can be studied by recording impulses in the long olfactory stalk of the catfish, the carp or the tench, as the nerve fibers of the stalk are medullated and are separated by only one synapse from the receptor cells.

2. The olfactory organs of these fish are sensitive to mechanical as well as to chemical stimulation. Chemical stimulation, which is brought about by various animal products, is most effective when the fluid contains solid matter in suspension.

Large rhythmic potential waves often appear in the forebrain, but in the olfactory bulb the connections between receptors and initial cells appear to form a series of independent pathways.

Hasama [204] in 1934 made string galvanometer records from the olfactory parts of the rabbit's brain and showed that these parts become electrically negative when a smell reaches the nose.

Changes in Number of Olfactory Fibers During Life.

Smith [205] examined 205 olfactory bulbs from 121 persons free from intracranial disease. By counting the number of olfactory glomeruli, he was able to estimate the number of fibers which reached a given bulb. The fibers began to disappear shortly after birth and continued to disappear at the rate of approximately 1 per cent a year. Some subjects had entirely lost the olfactory fibers at the age of 20, and few had a normal count after the age of 50.

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202. Proctor, B.; Lindsay, J. R., and Gonne, W. S.: Sequestration of the Osseus Labyrinth, Arch. Otolaryng. **37**:819-830 (June) 1943.

203. Adrian, E. D., and Ludwig, C.: Nervous Discharges from the Olfactory Organs of Fish, J. Physiol. **94**:441-460 (Dec.) 1938.

204. Hasama, B.: Ueber die elektrischen Begleiterscheinungen an der Riechsphäre bei der Geruchsempfindung, Arch. f. d. ges. Physiol. **234**:748-755, 1934.

205. Smith, C. G.: Age Incidence of Atrophy of Olfactory Nerves in Man: A Contribution to the Study of the Process of Ageing, J. Comp. Neurol. **77**:589-595 (Dec.) 1942.

Olfactory Tests in Health and Disease.

In 1935 Elsberg [206] described a procedure for examination of the olfactory sense. By introducing odorous substances into the nasal passages, he demonstrated in normal subjects that (1) a certain volume and (2) pressure of odor are necessary for recognition and identification of an odor. The minimum volume of an odor required for identification of the odor he called the "minimum identifiable odor" of the odorous substance. Furthermore, he found that injecting an odorous substance in a stream for a fixed period produced olfactory fatigue—inability to identify the odor when it was injected into the nasal passage in a blast. Normal subjects recovered from this olfactory fatigue within a definite number of minutes.

Minimal Volume for Identifiable Odor.—Two odorous substances were used—citral and coffee. These two substances were selected because their odors are familiar and easily recognized. The normal volume for the minimal identifiable odor of citral is between 3 and 9 cc. and that of coffee is between 5 and 10 cc.

Technic of Olfactory Tests: Elsberg's Tests in Routine Otologic Examination (Jones [207]).—In otolaryngologic work, "if the patient by sniffing cannot detect the odor of the substances mentioned [benzaldehyde, benzine, citral coffee, menthol, oil of turpentine and zylol] . . . the sense of smell is absent. If, however, he can detect any of these odors we can then undertake the [Elsberg] quantitative tests."

The blast test determines the threshold of sensation—the minimal identifiable odor, or M.I.O. It is the "olfactory coefficient," a number—the number of cubic centimeters of "air plus odor" required for the identification of the odor.

The stream test determines the fatigability of the sense of smell, and the effect of odor on the trigeminal nerve endings in the nose.

The Trigeminal and Olfactory Components in the Sense of Smell.—There are only three purely olfactory nerve odors, those of (*a*) coffee, (*b*) musk ketone and (*c*) phenylethylalcohol (Elsberg). Other substances produce stimulation of the trigeminal nerve endings. For the sense of smell is not only due to the effect on the olfactory end organs but most particularly due to the effect on the end organs of the first and second divisions of the trifacial, or fifth nerve. This "trigeminal component" is a great factor in what has hitherto been thought of as olfactory. The sense of smell, therefore, really includes both trigeminal and olfactory components (Jones [207]).

Comment (W. P. E.).—Jones's paper contains a succession of schematic drawings showing how aneurysms and tumors compress the central portions of the olfactory system.

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206. Elsberg, C. A., and Levy, I.: Sense of Smell: I A New and Simple Method of Quantitative Olfactometry, Bull. Neurol. Inst. New York **4**:5-19 (March) 1935. Elsberg, C. A.; Brewer, E. D., and Levy, I.: Sense of Smell: VII. The Odorous Substances to Be Used for Tests of the Olfactory Sense, ibid. **4**:286-293, (Oct.) 1935; V. The Relative Importance of Volume and Pressure of the Impulse for the Sensation of Smell and the Nature of the Olfactory Process, ibid. **4**:264-269 (Oct.) 1935.

207. Jones, I. H.: The Elsberg Precision Measurements of the Sense of Smell, Tr. Pacific Coast Oto-Ophth. Soc. **25**:197-216, 1940.

Pathways of the Olfactory-Parotid Reflex.

Peripheral Pathways.—Disturbances of the olfactory-parotid reflex occurring in patients with lesions of (*a*) the trigeminal or (*b*) the facial nerve suggest that these nerves are involved in the afferent arc of the reflex. The observation that the seventh cranial nerve is involved in the reflex may be suggestive of a relation to the fact that the large superficial petrosal nerve joins the facial nerve at the geniculate ganglion. Investigation of the relation of the facial nerve to the reflex might make it possible to distinguish peripheral lesions of the geniculate ganglion from central lesions.

Cerebral Pathways.—There is some evidence that the cerebral pathways which affect the reflex cross in their course from the cerebral cortex to the brain stem.

Contralateral Cerebral Cortex Has Greater Effect on Activity of Parotid Gland.—The cerebral cortex has a definite effect on salivary secretion (Pavlov [208] and von Bechterew [209]).

It appears likely that the contralateral cerebral hemisphere has a greater effect on the activity of a parotid gland than the ipsilateral hemisphere in man. In general, it was the impression of Elsberg and his associates that the function of the parotid gland contralateral to the cerebral lesion was more unstable and more abnormal than that of the parotid gland ipsilateral to the lesion.

Cerebral lesions, as Elsberg and his associates have shown, produce alterations in the resting rate of secretion and also in the reflex response of the parotid glands in a high percentage of patients with neurologic disorders.

Significance of Complete Anosmia.—The results of quantitative olfactory tests made on 1,000 patients were analyzed by Elsberg and Spotnitz.[210]

Of the 1,000 patients, 77, or 7.7 per cent, had complete anosmia. There was complete loss of the sense of smell in 23 of 195 patients with verified supratentorial tumors of the brain (12 per cent of the patients with tumor) and in 54 of the remaining 807 patients (6.7 per cent).

Therefore, if a patient with a supratentorial tumor of the brain has complete loss of the sense of smell, the probability is 91 per cent that the tumor is frontal, temporal or temporofrontal.

Results of Olfactory Tests Made on 128 of 239 Patients in Whom the Location of the Disease Was Certain.—In 91, or 71 per cent, of these

208. Pavlov, I. P.: Lectures on Conditional Reflexes, translated by W. H. Gantt, New York, International Publishers, 1928.

209. von Bechterew, W.: Die Funktionen der Nerven centra, Jena, Gustav Fischer, 1911, vol. 3.

210. Elsberg, C. A., and Spotnitz, H.: Value of Quantitative Olfactory Tests for Localization of Supratentorial Disease; Analysis of One Thousand Cases, Arch. Neurol. & Psychiat. **48**:1-12 (July) 1942.

the value for the minimal identifiable odor correctly indicated that the lesion was in or around the frontal lobe or an adjoining portion of the temporal lobe. In 5 patients (4 per cent) the olfactory localization was incorrect; in 10 (8 per cent) the localization was in doubt, and in 22 (16 per cent) there was no clinical evidence of an intracranial lesion.

Therefore, if a patient has symptoms of a supratentorial lesion and the olfactory test shows unilateral or bilateral elevation above the normal values for the minimal identifiable odor, the probability is 71 per cent that the lesion is on or around the frontal or the temporal lobe of the brain.

Summary: Unilateral or bilateral elevation of the value for the minimal identifiable odor alone occurred in from 38 to 45 per cent with lesions in or around the frontal or the temporal lobe. When patients with diffuse disease and those for whom a clinical diagnosis had not been arrived at were excluded, unilateral elevation of the value for the minimal identifiable odor occurred in from 71 to 78 per cent.

In 91 per cent of the patients with complete anosmia there was a tumor in or around the frontal or the temporal lobe of the brain.

In 81 cases of encephalic tumor, the correct side of the brain was indicated in 77 per cent, and the correct lobe in 80 per cent of these 77 per cent (Jones).

The Olfactory-Parotid Reflex in Disorders of the Central Nervous System.

Elsberg, Spotnitz and Strongin [211] made studies of (*a*) the effects of odorous substances on the secretory rate of the parotid glands, (*b*) the resting activity of the parotid glands, and (*c*) the effects of an odorous substance (citral) on the volume of secretion of each gland in persons with disorders of the central nervous system. They suggest that the reflex response of the parotid glands on stimulation of the nasal mucosa with odorous substances be called the olfactory-parotid reflex.

Rate of Secretion.—In normal persons the rate of secretion of the parotid glands is fairly regular. The average resting rate varies between 0.02 and 0.15 cc. Elsberg and associates calculated the average normal secretory rate of the two parotid glands for 50 subjects as being between 0.0421 and 0.0451 cc. per minute, or about 0.20 to 0.22 cc. for each five minute period.

The odorous substance, citral, when injected in a stream into the nasal cavity produced a definite increase in the volume of secretion from the ipsilateral parotid gland in normal human beings. The effect on the contralateral parotid gland was less marked. The resting rate of secretion of the parotid gland was found to be abnormal in 56 per cent of a series of 64 patients with neurologic disorders.

211. Elsberg, C. A.; Spotnitz, H., and Strongin, E. I.: The Olfactory-Parotid Reflex Study of One Hundred and Fifty Patients with Disorders of the Central Nervous System: A Preliminary Report, Arch. Neurol. & Psychiat. **47**:707-717 (May) 1942.

Diagnostic Differentiation Between Odors of Peripheral and Central Origins.

An evanescent odor that causes a patient great annoyance (Crosby and Farrior [212]) probably comes from a lesion in the upper air passages. Sustained presence of the noxious gas overtaxes the olfactory mechanism to exhaustion, with the result that the patient ultimately loses all consciousness of its presence.

On the other hand, when a patient complains of a constant impression of an odor, it is not peripheral, because the fatigue element enters early and obviates perception of a peripheral odor (Proetz [213]).

Organic lesions causing unpleasant olfactory perceptions of a fleeting nature are lesions of the uncinate convolution, in which are found the olfactory association centers. The patient exhibits a definite seizure, to which the term "uncinate attack" or "uncinate fit" has been given. Such an unpleasant odor is in the nature of a hallucination.

Meningioma of the olfactory groove presents a characteristic symptom complex of anosmia, papilledema and disturbances of the sensorium.

The characteristic symptoms of meningioma of the sphenoidal ridge include unilateral anosmia or hyposmia. Usually late manifestations of the disease may be associated with optic atrophy. Frequently the early signs of meningioma are unilateral proptosis with impairment of vision, and a central scotoma, the fundus revealing homolateral optic neuritis.

Tumors of the Temporal Lobe.—Approximately 20 per cent of tumors of the temporal lobe produce some form of olfactory disturbance, uncinate fits or attacks, indicating an irritative lesion somewhere within the region of the uncinate lobe. The attacks are characterized by "an evil smell" or "an evil taste."

Sachs, of St. Louis, reported 2 cases in which a tumor of the left temporal lobe completely destroyed the sense of taste and that of smell.

Uncinate Fits: Disturbance of Taste and Smell in Central Lesions.

The term "uncinate fit" (Hughlings Jackson, 1879) describes a type of epileptic seizure in which "at onset of paroxysms, a crude sensation of smell or one of taste" is a characteristic feature. Shenkin and Lewey [214] state that the portion of the cerebral cortex responsible for this aura or sensation of taste is the hippocampal gyrus and its uncus, situated in the basal surface of the temporal lobe, the cortical representation of taste being linked with that of smell (Shenkin).

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212. Crosby, E., and Farrior, B.: Neurologic Lesions Which Influence the Sense of Smell, Arch. Otolaryng. **38**:529-530 (Nov.) 1943.

213. Proetz, A. W., in discussion on Crosby and Farrior.[212]

214. Shenkin, H. A., and Lewey, F. H.: Aura of Taste Preceding Convulsions Associated with a Lesion of the Parietal Operculum: Report of a Case, Arch. Neurol. & Psychiat. **50**:375-378 (Sept.) 1943.

While evidence points to the uncinate localization of the sense of smell, there is no evidence for a localization of the sense of taste.

Parietal Operculum, Center for Taste.—Bornstein has shown that anatomic and physiologic data point to a cerebral representation of the sense of taste (*a*) separate from that of the sense of smell and (*b*) associated with tactile sensibility of the tongue—an area in the inferior part of the postcentral gyrus, the so-called parietal operculum (cover or lid).

A Case of Gustatory Aura Supporting the Theory That the Taste Sense Is Represented in the Parietal Operculum (Shenkin and Lewey).—The patient, a man aged 27, had recurrent headaches and easy fatigue for two months. During this period he had four generalized convulsive seizures, each preceded by an aura of a sour-bitter taste.

The perception of sweetness was absent over the left side of the tongue. Bitter and salt substances were normally recognized over the entire tongue.

Operation revealed a congeries of large engorged vessels located in the sylvian fissure. The point of greatest dilatation of these vessels was over the lowest portion of the posterior central gyrus.

In discussion of this case W. S. Bornstein stated that the jacksonian attacks were initiated by hallucinations of taste on the half of the tongue opposite the side of the lesion.

Cortical Anorexia.—One of Bornstein's patients with severe impairment of the sense of taste had also lost his formerly good appetite, as a result of a bullet wound. The phenomenon of "cortical anorexia," together with hypogeusia, persisted until his death, six years after the injury.

As a rule, taste has bilateral representation, with numerical predominance of the opposite side.

Syndrome of the Central Operculum (Bornstein).—The "syndrome of the central operculum" is characteristic of lesions in the neighborhood of the cortical taste area: (*a*) impairment of chewing and (*b*) hypersalivation, (*c*) sensory (and motor) impairment of tongue, mouth, lips and thumb, and (*d*) motor aphasia (Bornstein).

Defects of Smell After Injury of the Head.[215]

Ogle described 3 cases of anosmia consequent to injury of the head, the loss being due to rupture of the olfactory nerves as they pass from the olfactory bulb through the ethmoid bone.

Goland (1937) suggested with Legg (1873) that the loss results from damage of the lateral olfactory stria and tip of the temporal lobe by impact against the lesser wing of the sphenoid bone.

215. Leigh, A. D.: Defects of Smell After Head Injury, Lancet **1**:38-40 (Jan. 9) 1943.

Of 1,000 patients consecutively examined because of injury of the head, 72 (7.2 per cent) had impairment of the sense of smell. Of the 72 patients, 41 had complete anosmia, 31 presented general diminution of olfactory acuity or unilateral anosmia and 12 complained of parosmia.

The onset of post-traumatic parosmia was usually delayed from seven days to three months.

Disturbances of Taste After Injury of the Head.—Of the entire group of 72, only 14 complained of disturbance in taste, indicating that the connection between taste and smell is not so close as has been popularly supposed.

The inconstant association of the loss of taste and the loss of smell in most cases is not fully explained. Perhaps taste is more affected by olfactory stimuli in some persons. In addition to the tearing of the olfactory filaments, there may be damage of the temporosphenoidal lobe or of the region of the anterior perforated crater. Also, taste fibers may be concomitantly affected in their course through the petrous bones. Seven of the 14 patients with disturbance of taste showed a fissured fracture extending directly from the parietotemporo-occipital region toward the base and had other signs of possible petrous damage.

ENCEPHALOMENINGOCELE IN THE NASAL CAVITY

"All congenital extracranial tumors containing both brain tissue and meninges should be classified as 'encephalomeningoceles'" (Ballenger).

Encephalomeningocele in the nasal cavity is a cystic tumor containing brain tissue, meninges and cerebrospinal fluid, enclosed in fibrous walls and covered with nasal mucosa. It may be mistaken for a fibroma or a polyp. It is usually connected with the brain by a pedicle that passes through a dehiscence in the cribriform plate.

It is a rare condition, the literature containing reports of only 9 authentic cases. In all but 2 death occurred from meningitis following operation.

McGillicuddy [216] is of the opinion that reported cases of meningitis and death following removal of "what seemed to be" a benign polyp were probably cases of encephalomeningocele (Dahmann and Müller's [217] case, 1925).

McGillicuddy's Case of Recovery After Snare Removal and Chemotherapy, with Meningitis One Year Later.—A patient aged 13 years had a large intranasal encephalomeningocele which caused disfigurement by protruding from the nose.

A roentgenogram revealed changes in the cribriform region suggesting erosion or "possible developmental disturbance."

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216. McGillicuddy, O. B.: Encephalomeningocele in the Nasal Cavity, Arch. Otolaryng. **36**:447-448 (Sept.) 1942.

217. Reviewed, Eagleton, W. P.: Eagleton's Index and Abstracts of Literature on Progress in Intracranial Lesions Related to Aural and Nasal Conditions, Newark, N. J., 1941, reprint (1928), p. 8.

The tumor was removed intranasally with a tonsil snare and wire, the pedicle being cut by slow pressure. Histologic examination showed encephalomeningocele with a firm fibrous stroma. Large doses of sulfanilamide were given for two weeks. The nasal obstruction and deformity were relieved, but drainage from the left nostril continued. However, the discharge, which had been mucoid or sometimes purulent before operation, was now clear.

"Nearly a year" after operation, the nasal discharge ceased, and symptoms of meningitis developed. Azosulfamide injected intramuscularly and sodium sulfapyridine administered intranasally produced prompt recovery. The nasal discharge has been much diminished since recovery.

Classification of Congenital Hernias of the Skull.[218]

Heineke [219] in 1882 divided congenital hernias of the skull into three groups: first, basal, emerging through any part of the cribriform plate into the nasal cavity; second, sphenopharyngeal, leaving the cranium through an opening between the sphenoid and the ethmoid bones and hanging in the choanal region of the nasal cavity; third, hernias entering the nasopharynx through defects between the sphenoid and occipital bones.

Intranasal Variety.—In 1932, Hallermann [220] could find only 8 cases recorded in the literature. All had been reported prior to the advent of chemotherapy, and all resulted fatally with the exception of Fenger's [221] case of a large sphenomaxillary encephalocele. This occurred in an adult and was operated on successfully by resecting the superior maxilla and ligating the pedicle.

McGillicuddy found another authentic case, reported by Rocher and Anglade [222] in 1924: An intranasal tumor was successfully removed from a 3 day old infant by snare.

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218. Guthrie, D., and Dott, N.: The Occurrence of Brain-Tissue Within the Nose: The So-Called Nasal Glioma, J. Laryng. & Otol. **42**:733-745 (Nov.) 1927; abstracted, Eagleton, W. P.: Eagleton's Index and Abstracts of Literature on Progress in Intracranial Lesions Related to Aural and Nasal Conditions, Newark, N. J., 1941, reprint (1928), pp. 7-8.

The authors suggest the term "encephaloma" for some of these tumors.

Rawling, L. B.: Congenital and Traumatic Cysts of the Brain and Meninges, St. Barth. Hosp. Rep. **40**:75-92, 1904.

Lampert, F. M.: Pathogenesis and Treatment of So-Called Congenital Cerebral Hernia, Surg., Gynec. & Obst. **38**:159-162 (Feb.) 1924.

219. Heineke, W.: Die chirurgischen Krankheiten des Kopfers, Stuttgart, F. Enke, 1882.

220. Hallermann, O.: Intranasale Meningocelen und ihre klinische Diagnose Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:413-420, 1932.

221. Fenger, C.: Basal Hernias of the Brain, Am. J. M. Sc. **109**:1-17 (Jan.) 1895.

222. Rocher, H. L., and Anglade: Les fibrogliomas de la region nasale, Rev. de chir. **62**:147-178, 1924.

FACIAL PARALYSIS CAUSED BY INFECTIOUS NEURITIS FOLLOWING A MILD INFECTION OF THE RESPIRATORY TRACT

Infectious polyneuritis or neuronitis (Sabin and Aring [223]) is characterized by widespread motor and sensory signs pointing to involvement of spinal and cranial nerves, most commonly the seventh nerve. Signs usually appear days or weeks after a mild infection of the respiratory tract. The cerebrospinal fluid shows a marked increase of protein.

A member of the pleuropneumonia group of filtrable microorganisms of mice can produce a toxin with selective affinity for specific parts of the nervous system. The visceral pathologic changes appear in (*a*) the adrenal glands (mainly focal degeneration and mononuclear cell infiltration), (*b*) the liver (focal cellular infiltration of the capsules and portal spaces, focal necrosis with cellular infiltration, and focal fatty degeneration of the liver cells), (*c*) the kidneys (focal intertubular infiltration with mononuclear cells), (*d*) the heart (interstitial infiltration with mononuclear and polymorphonuclear cells).

In 1 case a vessel in the glomerular layer of one of the olfactory bulbs had perivascular cuffing with round cells.

Sabin and Aring express the belief that infectious polyneuritis is caused by a toxin or toxins which have affinities (1) for the peripheral nerves, especially the seventh nerve, and (2) for the viscera. Furthermore, the polyneuritis is aggravated by the micro-organisms responsible for the infection of the respiratory tract usually preceding the onset of nervous symptoms.

SUPPURATIVE LESIONS OF THE PITUITARY GLAND FROM NASAL INFECTIONS

Unsuspected Abscess of Nasal Origin in the Sella Turcica.

Svien and Love [224] report this interesting case:

A 34 year old woman complained of severe headache, vomiting and excessive thirst dating from a postpartum period thirteen years before. Nasal obstruction with polyps had been present "off and on" for sixteen years.

Examination showed a perforation of the right drum membrane. "Pale polyps" filled the right nasal cavity. There was bitemporal hemianopsia. A roentgenogram revealed the "sella turcica enlarged" with "erosion of the floor in the anterior portion."

The diagnosis was "chiasmal lesions" due to "pressure from the sella and the optic chiasm."

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223. Sabin, A. B., and Aring, C. D.: Visceral Lesions in Infectious Polyneuritis, Am. J. Path. **17**:469-482 (July) 1931; abstracted, Neuro-Psychiatric Institute, Hartford Retreat, Dec. 3, 1941, series 9, no. 179.

224. Svien, H. J., and Love, J. G.: Abscess Within the Sella Turcica Simulating Pituitary Tumor: Surgical Cure, Proc. Staff Meet., Mayo Clin. **17**:497-501 (Sept. 23) 1942.

Right transfrontal craniotomy was performed to remove the pressure. "At operation we were surprised to find pus; then, having found it, we were . . . in somewhat of a quandary as to what to do next. . . ." Here "we were faced with an abscess which opened into all the basal cisterns, which meant that it was impossible to wall it off. . . . Hence . . . [after the pus had been evacuated] we placed sulfanilamide inside the cranium and packed it into the sella turcica. It was our opinion that the risk of packing sulfanilamide around the optic nerves was less than the risk of leaving active micro-organisms at the site of operation, because at the time of operation we naturally assumed that there were organisms in the pus we encountered."

Vascular Spasm of the Right Side of the Circle of Willis from Direct Packing of Crystals of Sulfanilamide into a Latent Abscess of the Pituitary Region Caused by Nasal Infection.—On the seventh day in the case described there was a sudden attack of left hemiplegia, involving the face, and anesthesia; all vanished spontaneously within several days, the only residuum being facial weakness at the time of the patient's dismissal on the eighteenth postoperative day. It was the consensus that the patient had had a vascular spasm involving the right side of the circle of Willis.

Why Meningitis Did Not Develop.—"It might be assumed . . . that the patient recovered because of the presence of the sulfanilamide; yet we do not think such an assumption would be justified, because culture of the pus was negative. We should be more inclined to consider that the complications which this patient experienced were due to the sulfanilamide, because we have no other explanation for them."

After Treatment of Diabetus Insipidus by Nasal Insufflations.—Subsequently "the diabetes insipidus was well controlled by nasal insufflations of pituitary powder."

Cavernous Sinus Thrombophlebitis from a Furuncle of the Nose Complicated by Small Cerebral Infarctions, Purulent Leptomeningitis, Bilateral Orbital Abscesses and Infarction of the Pituitary Gland (Weisman [225]).

The unique features were the multiple foci of necrosis in the left cerebral hemisphere and the necrosis of the pituitary gland.

Necrosis of the pituitary gland has not previously been described in cases of cavernous sinus thrombophlebitis. No symptoms of pituitary insufficiency were observed in the patient. About 75 per cent of this gland was infarcted. According to Sheehan, 50 per cent or more of the pituitary gland must be lost before clinical evidence of deficiency appears.

The distribution of the lesions and the finding of occluded arteries left no doubt that the lesions were arterial infarcts. The absence of primary arterial disease and the abrupt onset of the cerebral symptoms suggest embolic occlusion. Another

225. Weisman, A. D.: Cavernous Sinus Thrombophlebitis: Report of a Case with Multiple Cerebral Infarcts and Necrosis of the Pituitary Body, New England J. Med. **231**:118-122 (July 27) 1944.

possibility is that the arteries became thrombosed as a result of the contiguous leptomeningitis, but it is difficult to see how this could have occurred without accompanying thrombosis of the thinner-walled veins.

Within the cavernous sinus the internal carotid arteries showed local arteritis. Polymorphonuclear leukocytes had invaded the coats of these arteries, and over such inflammatory foci there was marked intimal proliferation. These arterial lesions correspond to the experimental infectious angiitis of Winternitz and Le Compte, who by injecting Staph. aureus produced necrosis in the wall of a vein, as well as thrombosis and acute arteritis with intimal hyperplasia in an adjacent artery. There was no evidence of thrombosis.

The signs of involvement of the ophthalmic division of the trigeminal nerve (frontal headache and blunting of sensation over the cornea and the forehead) were probably the result of toxic damage and edema.

Fatalities from Infections of the Paranasal Sinuses.

Salinger [226] has made a survey of the literature on involvement of the paranasal sinuses. Ray and Parsons [227] present the histories of 3 cases, all of which came to autopsy. The most important factors are osteitis of the posterior wall of the frontal sinus and thrombophlebitis of small veins in the mucosa of the sinus. The latter furnish the pathways by which infection may extend to the dura long before the intervening bone has succumbed. Most of the data at hand seem to indicate that the subdural space is infected by direct penetration of the dura itself.

Two of Piquet's [228] patients survived under treatment with sulfonamide compounds; the others died. The operations which preceded meningitis included removal of a small intranasal growth with a snare, resection of a septum, intranasal ethmoidectomy and external operation for a carcinoma of the ethmoid labyrinth involving the orbit.

In Spencer-Harrison's [229] patient, it was shown at autopsy, the infection reached the meninges from the sinus by way of the infra-orbital canal.

Chronic Nasal Sinusitis as a Cause of Acute Mental States.

Russell's [230] conclusions are: 1. Mental disorder is commonly associated with chronic systemic disease.

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226. Salinger, S.: Paranasal Sinuses, Arch. Otolaryng. **40**:307-324 (Oct.) 1944.

227. Ray, B. S., and Parsons, H.: Subdural Abscess Complicating Frontal Sinusitis, Arch. Otolaryng. **37**:536-551 (April) 1943.

228. Piquet, J.: Die Sulfamidbehandlung in der Prophylaxe der postoperativen Meningitis, Monatschr. f. Ohrenh. **76**:68-75 (Feb.) 1942.

229. Spencer-Harrison, M. E.: Infection of the Meninges in Maxillary Sinusitis, J. Laryng. & Otol. **58**:196 (May) 1943.

230. Russell, H. G.: Sinus Trouble and Personality, J. Ment. Sc. **87**:479-513 (Oct.) 1941.

2. The lining of the pneumatic cells of the head responds to streptococcic infection by producing edema. Sinusitis of etiologic importance commonly occurs without production of pus.

3. Allergy with inflammation may cause great and rapid swelling of the mucosal lining of the sinuses, occluding the ostiums.

4. The changes of pressure thus induced promote the absorption of toxins which are forced through the haversian canals in the bone separating the sinuses from the neighboring cavities, notably the cranial cavity.

Pathologic Aspects.—The four following observations indicate some of the ways in which toxic fluid absorbed from the sinuses may affect the neighboring parts.

1. If a solution of indigo carmine (Yates, 1924) is instilled into a healthy human sinus, the dye can be seen some minutes later being swept down along recognizable ciliary paths on the surface of the mucosa of the posterior pharyngeal wall.

However, if the sinal lining has been harmed by infection, the dye is not swept out but can be recognized in tiny blue lines on the pharyngeal wall *under the mucous membrane.* It has been absorbed through the mucosa and is in the lymphatics of the submucosa. It appears in the urine in twenty minutes. This suggests why nephritis and fibrositis are frequently associated with sinusitis.

2. If particulate blue dyes (to resemble micro-organisms) are instilled into the noses of a series of rabbits and the animals killed at hourly intervals, after one hour the *olfactory lobes and neighboring parts of the brain may be stained blue (Le Gros Clark, 1929).*

3. If a 20 per cent cocaine solution (Sluder, 1919) is instilled into the human sphenoid sinus, there follows, in many cases, sensory palsy of the area supplied by the trigeminal nerve on that side. In many persons the gasserian ganglion is in very close anatomic relationship with the sphenoid sinus, in the upper and outer wall of which there is, in a small percentage of cases, a hiatus in the bone (Ferris Smith, 1934), so that the meninges are in contact with the sinal lining. This experiment gives a suggestion of the way in which sphenoid sinusitis may affect the trigeminal nerve.

4. Even in the absence of a hiatus toxin may be rapidly absorbed from the sphenoid sinus in the brain. Ferris Smith in a personal communication cited a case in which the sphenoid cavity was swabbed out with a solution containing trinitrophenol (picric acid). The patient died of heart failure the same night. At autopsy the lower parts of the brain were found deeply stained yellow.

Recrudescence of Sinusitis Caused by Trauma and Allergy in the Production of Meningitis.—The "stirring-up of secondary foci" is exemplified in the production of meningitis. There is definite evidence that the meninges are subject to being peacefully penetrated over long periods by organisms from chronic foci of infection in the sinuses, including the middle ear–cleft group, and it is possible that the meninges become sensitized to these organisms, acute meningitis being a kind of allergic response to a fresh wave of infection in the sinuses.

Groups of Mental Symptoms from Sinusitis.—(*a*) Attacks of dizziness and instability persisting after obstruction of the eustachian tubes has been relieved.

Giddiness amounting to inability to walk without support was cured for a year by drainage of the right sphenoid sinus. Later recurrences of this symptom were immediately relieved by lavage of the opposite sphenoid sinus and were finally cured (now five years) by left sphenoidostomy.

(*b*) Attacks of "losing oneself" or "blackouts." In such cases it is usual to find roentgenographic evidence of posterior sinus block.

In 1 case some weeks after sphenoidostomy it was possible by applying suction or pressure to the sphenoid cavity to reproduce the "blackouts" from which the patient had suffered since childhood and which have not recurred (five years).

(*c*) Attacks of transient blindness.

This was demonstrated in 1 case only. Raising of pressure in a posterior ethmoid cell by syringing at once produced homolateral blindness with severe headache.

(*d*) Referred pain from the trigeminal nerve.

The trigeminal nerve is responsible for the nerve supply of the greater part of the meninges, as well as that of the mucous membrane of the sinuses and that of the teeth, the tongue and the surface of the face and head. Consequently pain may be referred, for example, from tooth to scalp. But it seems not so well recognized that pain may be referred from sinus or tooth to meninges.

(*e*) Severe mental states caused by sinusitis.

A man aged 45, when asked his complaint, said, "I suffer from strongly homicidal tendencies whenever my nose goes wrong." After the removal of a foul-smelling rhinolith from his right nasal passage, his symptoms remained in abeyance for two years.

Another man with sphenoiditis had homicidal tendencies. In association with sudden attacks of pain in the right side of his head he had on several occasions made unpremeditated and unwarranted attacks on people, the last being on an unoffending friend. A roentgenogram made after replacement with iodized poppy-seed oil 40 per cent showed the right sphenoid sinus blocked and opaque.

Watson-Williams,[231] of Bristol, England, in discussion said: "There is a sort of mental lassitude; the victim finds that the effort demanded by social duties is becoming too great; work which formerly he performed with ease and pleasure has become laborious; when he forces himself to work he cannot concentrate his mind; he feels he has lost his initiative; memory may fail or more typically may become 'patchy'; and to make a decision on some quite minor matter involves a disproportionate effort." It was this collection of symptoms, evidence of sluggish or failing mentality, that Watson-Williams had come to regard as probably due to toxic absorption, largely because thorough treatment of the lesions that might cause such absorption had often—indeed almost regularly—led to relief.

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231. Watson-Williams, E.: Aural Focal Sepsis as Source of Neurasthenia and Insanity, Brit. M. J. **2**:10-11 (July 4) 1925.

UNUSUAL COMPLICATIONS OF MASTOIDITIS

Vague Neurologic Symptoms in a Few Cases of Uncomplicated Mastoiditis.

Trowbridge [232] studied 112 patients with uncomplicated mastoiditis. Positive neurologic signs occurred in only a few patients. They included (*a*) headaches, (*b*) nausea and vomiting, (*c*) changes in the ocular fundi and (*e*) involvement of cranial nerves.

The optic fundi were examined in 91 patients; they were normal in 83 (91 per cent). Hyperemic changes were present in the fundi of 8 patients (9 per cent).

Of 95 patients examined, 25 (26 per cent) presented horizontal nystagmus of varying quality.

Facial Paralysis.—Three patients had preoperative and 5 postoperative peripheral seventh nerve palsies on the side on which operation was performed. One patient with sixth nerve palsy on the side contralateral to the operative side recovered in a few days.

The lumbar fluid pressure was normal (90 to 200 mm. of water) in 78 of 91 examined, moderately elevated (200-250 mm. of water) in 12 and high (440 mm. of water) in 1 patient.

Fatal Intracranial Hemorrhage Following Mastoidectomy.

Suggit [233] reports a case in which, following mastoidectomy, a hemorrhage from the lateral sinus stripped the dura mater off the floor of the middle cranial fossa, giving rise to symptoms simulating a space-occupying lesion in the temporal lobe.

The patient, a man aged 33, had suffered from bilateral intermittent disease of the middle ear since childhood. He had had a posterior perforation of the left drum membrane with discharge and pain for three weeks. The right drum membrane showed a dry central perforation.

The left mastoid process was opened. Both the lateral sinus and the middle fossa were widely exposed; they appeared healthy.

Seven hours after operation the dressings became soaked. An hour and a half after the wound had been repacked, the pulse rate had fallen to 42; there was no further bleeding.

The following morning the patient was partially aphasic, with slow, perseverating speech. There was ptosis of the left eye. He was not moving the right leg as well at the left. The gauze pack was removed, and blood welled up. The bleeding was controlled by a fresh back.

In the afternoon there was complete palsy of the third cranial nerve on the left side, a partial supranuclear paralysis of the right seventh nerve and hypotomy of the right arm and leg; the abdominal reflexes were absent on the right side, and the right plantar response was extensor.

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232. Trowbridge, E. H., Jr.: Neurological Aspects of Simple Mastoiditis, J. Nerv. & Ment. Dis. **95**:575-579 (May) 1942.

233. Suggit, S.: Extradural Haemorrhage in the Middle Fossa Arising from the Lateral Sinus, J. Laryng. & Otol. **58**:117-119 (March) 1943.

The provisional diagnosis was "a space-occupying lesion of the left temporal lobe probably due to a sudden increase of oedema, following the mastoid operation, surrounding a chronic brain abscess."

The third day after operation the patient was more aphasic, the pulse rate, 100.

A left temporal osteoplastic flap was raised and the dura incised. The brain was suffused, purplish red and under tension. No abscess was found with the exploring needle. The osteoplastic flap was replaced.

Death occurred twelve hours later.

Postmortem examination revealed an extensive extradural clot occupying the left middle cranial fossa, the dura being completely stripped from the floor of the middle fossa. But the clot did not reach the level of the osteoplastic flap.

A softening of the wall of the lateral sinus was encountered, through which a probe passed into the blood clot.

In connection with this case Watkyn-Thomas [234] recalled seeing a man a few hours after an injury, the man having fallen. There was a large bruise over the right mastoid region. The man was semiconscious. He had paralysis of the sixth cranial nerve, facial weakness and loss of abdominal reflexes on the right side and some weakness of the left arm. The pulse rate was 50, and an hour later 46, with a systolic blood pressure of 150 mm. of mercury. When a disk of bone was removed, a depressed fracture of the inner table with a tear in the wall of the lateral sinus and a large extradural clot were revealed. The rent in the lateral sinus was patched with a strip of muscle.

It is suggested that the mechanism by which extradural hemorrhage arises is an obstruction of the distal or cardiac end of the lateral sinus by clot, with free bleeding from the proximal or cranial end. The essential features leading to a correct diagnosis are the sudden occurrence of signs of compression of the temporal lobe and a marked and sudden slowing of the pulse.

THE CEREBROSPINAL FLUID SYSTEM IN RELATION TO DISEASES OF THE NOSE AND THE EAR

Effects of Increased Intraventricular Pressure on Respiration and Circulation [235]; Danger of Lumbar Puncture When There Is a Block Between the Ventricular Fluid Pressure and the Subdural Fluid Pressure.

In addition to the Monro-Kellie hypothetic limited elasticity of the dural sac [236] there is adjustment to changes of blood volume in the brain tissue, which may take place as follows: Cerebrospinal fluid is displaced from the subarachnoid and ventricular reservoirs in the cranial cavity, through the foramen magnum and into the spinal portion of the dural

234. Watkyn-Thomas, F. W.: Personal communication to Suggit. [233]

235. Kahn, A. J.: Effects of Variations in Intracranial Pressure, Arch. Neurol. & Psychiat. **51**:508-527 (June) 1944; correction, ibid. **52**:71 (July) 1944.

236. Flexner, L. B.; Clark, J. H., and Weed, L. H.: Elasticity of Dural Sac and Its Contents, Am. J. Physiol. **101**:292-303 (July) 1932. Weed, L. H.: Some Limitations of Monro-Kellie Hypothesis, Arch. Surg. **18**:1049-1068 (April) 1929; Positional Adjustments of Pressure of Cerebrospinal Fluid, Physiol. Rev. **13**:80-102 (Jan.) 1933.

sac. The rise in systemic blood pressure thus leads to increased cerebral volume. This dependence of the volume of the brain on the level of the systemic blood pressure was first shown by Roy and Sherrington [237] in 1898.

Respiratory and Circulatory Effects.—In Kahn's [235] experiments no circulatory or respiratory embarrassment occurred when both the cisternal and the intraventricular pressure were at high levels, but medullary embarrassment appeared soon after the cisternal pressure was lowered while the intraventricular pressure remained high.

The ill effects of high intraventricular pressure in the presence of low cisternal pressure are due to the circumstance that the medulla herniates into the foramen magnum. This herniation was experimentally observed in dogs consequent to elevation of the intraventricular pressure while the cisterna magna was opened to the exterior. The possibility also exists that the mesencephalon herniates through the incisura tentorii and that the respiratory and circulatory effects were due to this.

When the intracerebral and the intraventricular pressures approached the level of the diastolic blood pressure, death resulted from respiratory and circulatory failure.

Effects of Raised Intracranial Pressure on Consciousness.—The experiments on the dog were made with the intention of studying the effect of experimentally produced cerebral edema on consciousness.

Comment (Kahn).—The ill effects from high intraventricular and low cisternal pressure disappear when the disparity between the two pressures is reduced. "This indicates the danger involved in lumbar puncture when the possibility of a block between the ventricular reservoir and the subdural fluid spaces exists."

In the presence of such a block the cisternal pressure is of no value in determining the level of intracerebral (within the brain tissue) or intraventricular pressure (internal hydrocephalus).

Perivascular Lymphatic-Connected Space in the Formation of Sinus Thrombus and Encephalic Abscess.

A series of papers by Griffith and associates [238] present evidence somewhat at variance with the commonly accepted theory as to how

237. Roy, C. A., and Sherrington, C. S.: On Regulation of the Blood-Supply of the Brain, J. Physiol. **11**:85-108, 1890.

238. Griffith, J. Q., Jr.; Jeffers, W. A.; Fewell, A. G., and Fry, W. E.: A Study of the Communication and Direction of Flow Between Cerebrospinal Fluid and Optic Discs in the Rat, Am. J. Ophth. **20**:457-461 (May) 1937. Griffith, J. Q., Jr.; Fry, W. E., and McGuinness, A.: Experimental and Clinical Studies in Hydrocephalus, Am. J. Ophth. **23**:245-251 (March) 1940. Griffith, J. Q., Jr.; Jeffers, W. A., and Lindauer, M. A.: A Study of the Mechanism of Hypertension Following Intracisternal Kaolin Injection in Rats, Am. J. Physiol. **113**:285-290

(Footnote continued on next page)

cerebrospinal fluid is absorbed from the cerebrospinal space. The accepted theory is summarized from papers of Weed [239] and Fay,[240] by Garlichs and Griffith [241] as follows: "Fluid leaves the blood stream and passes through the choroid plexus to form the bulk of the cerebrospinal fluid. A lesser amount leaves the capillaries of the brain to become the intercellular fluid of the brain, which . . . is finally drained off, either into the capillaries of the brain or along the perivascular spaces, through which it reaches the subarachnoid space, to add a final minor increment to the cerebrospinal fluid."

"Absorption of cerebrospinal fluid occurs: (1) mainly into the blood stream, . . . largely through . . . the pacchionian bodies lying in the walls of the [venous] sinuses, especially the superior longitudinal sinus, through which fluid passes directly from the subarachnoid space into the lumen of the sinus, and (2) to a lesser and minor extent along the perineural spaces, leading to the systemic lymph nodes."

Garlichs and Griffith [241] then summarize their modified view: "1. The pacchionian bodies and special sinus structures have no function in effecting absorption of cerebrospinal fluid." What fluid is absorbed into the blood stream, "enters vessels of capillary size," . . . 2. "An important . . . part of the cerebrospinal fluid" is absorbed through perineural or perivascular channels, "which lead to systemic lymphatics. This mechanism may be described as lymphatic absorption . . . [The correctness of this view was denied by Weed, W. P. E.]

"The route for particulate matter released over the hemispheres of the brain" is "along perivascular spaces to the perisinal space of the superior longitudinal sinus and thence along corresponding spaces of the torcular Herophili, the lateral sinus and the jugular vein, to reach finally the cervical lymph nodes."

"If this view is correct, the perisinal spaces must be considered in problems of infection of the cerebrospinal space and its coverings. The present study deals with the relation of the perisinal space of the lateral sinus to lymphatic absorption from the auditory bulla of the rat. The auditory bulla was selected because, in some respects, it is analogous to the mastoid process of man. It is a bony

(Oct.) 1935. Griffith, J. Q., Jr., and Roberts, E.: Further Studies in the Mechanism of Vascular Hypertension Following the Intracisternal Injection of Kaolin in Rat, ibid. **124**:86-93 (Oct.) 1938.

239. Weed, L. H.: Certain Anatomical and Physiological Aspects of the Meninges and Cerebrospinal Fluid, Brain **58**:383-397 (Sept.) 1935.

240. Fay, T.: Generalized Pressure Atrophy of the Brain Secondary to Traumatic and Pathologic Involvement of Pacchionian Bodies, J. A. M. A. **94**:245-249 (Jan. 25) 1930.

241. Garlichs, R. W., and Griffith, J. Q., Jr.: Lymphatic Absorption from Auditory Bulla of the Rat, with Special Reference to the Lateral Sinus, Arch. Otolaryng. **32**:226-231 (Aug.) 1942.

structure containing air-filled spaces and lies in close relation to the lateral sinus of the same side."

Summary (Garlichs and Griffith).—Lymphatic absorption occurs "along the perisinal space of the lateral sinus." In the course of an acute infection, it is assumed, the following events may take place:

"1. The infection may involve the wall of the sinus, causing a mural thrombus, which may give rise to septic emboli and general infection of the blood stream. This thrombus may occur at a considerable distance from the original focus of infection.

"2. The thrombus may completely block the lumen of the sinus, leading to the usual intracranial signs of sinus thrombosis, or even abscess of the brain.

"3. The infection may block the normal route of perisinal absorption from the cerebrospinal space, . . ."

Clinical Conclusion from Drainage of Spinal Spaces by Exposure of the Lateral Sinus.—"Surgical exposure of the sinus provides drainage of the perisinal space and should prevent further spread of the infection. This may explain the numerous cases in which the following sequence of events has been observed clinically: (1) presence of mastoid disease; (2) clinical signs of intracranial extension; (3) operation, with observation of a diseased mastoid and a normal lateral sinus, and (4) rapid recovery."

Deafness Caused by Quinine Present in the Cerebrospinal Fluid of the Newborn Infant as a Result of the Mother's Taking the Drug.

Quinine-induced deafness of newborn infants is now "an accepted entity." Quinine and its salts exert their influence "directly upon the sense organs" . . . especially on "the external hair cells of the organ of Corti." Thus quinine "may imperil the delicate aural mechanism not only of adults and children but of the fetus in utero as well, through its presence in the maternal circulation" (Taylor and associates [242]).

Taylor, Dyrenforth and Pollard argue that because of the deleterious action of quinine on (*a*) the ganglion cells of the cochlea and (*b*) the endothelium of the small blood vessels of the internal ear, and, furthermore, because of its (*c*) tendency to diminish the pressure in the endolymph, there results a series of events culminating in ischemia, anoxemia, lack of nutrition and eventual degeneration of the ganglion cells and the nerve fibers in the basal coil of the cochlea.

The "presence of quinine in the cerebrospinal fluid of the newborn infant is *a priori* evidence of its contact with the finer structures of the organ of hearing."

242. Taylor, H. M.; Dyrenforth, L. Y., and Pollard, C. B.: Absorption of Quinine into the Cerebrospinal Fluid of the Fetus in Utero, Ann. Otol., Rhin. & Laryng. **50**:1030-1037 (Dec.) 1941.

Its "presence in the cerebrospinal fluid suggests an important analogy between the stria vascularis, which elaborates the endolymph, and the choroid plexus, which is responsible for the secretion of the cerebrospinal fluid." The "hair cells of the organ of Corti may be bathed in endolymph containing quinine."

"The basis for this reasoning is threefold: (1) the known permeability of the fetal-maternal membranes for crystalloid substance, (2) the findings by various investigators of quinine and other drugs in the blood serum and excreta of animals following their administration to preparturient mothers, and (3) the unmistakable evidence, both clinical and histologic, of damage to the internal ear of such fetuses."

The observations of Taylor, Dyrenforth and Pollard are based on the examination of 7 women about to become mothers.

Technic.—At the first indication of the onset of labor the expectant mother was given quinine bisulfate orally—5 grains (0.32 Gm.) of the salt was given three or four times a day.

Forty-eight hours after birth, each of the 7 infants was carefully subjected to lumbar puncture.

To detect quinine in the cerebrospinal fluid, 2 Gm. of ammonium sulfate was added to 8 cc. of cerebrospinal fluid from the infant, and the solution was made alkaline with ammonium hydroxide. It was then extracted four times with ether and the extracts evaporated. The residue was taken up with a few drops of hundredth-normal acetic acid, and distilled water was added to bring the volume to 1 cc. Abenson's erythroquinine test was positive on this preparation.

Even a low maternal intake of 30 grains (1.94 Gm.) was sufficient to produce positive results in the fetal cerebrospinal fluid and urine.

News and Comment

FIRST PAN-AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHO-ESOPHAGOLOGY

A meeting of the Pan-American Congress of Otorhinolaryngology and Broncho-Esophagology will be held in Chicago in October 1946, sponsored by the American Academy of Ophthalmology and Otolaryngology, with the cooperation of the societies of otorhinolaryngology of the other American republics and Canada. This meeting will follow immediately after, and overlap, the annual meeting of the American Academy of Ophthalmology and Otolaryngology. Those attending the Pan-American Congress from other countries will be invited to participate as guests in the scientific and social activities of the meeting of the Academy. All otorhinolaryngologists of good standing in North, Central and South America and the West Indies are invited to attend.

Transportation and Hotel Accommodations; Registration.—The Pan-American Airways and connecting railways, as well as railroad and steamship lines, will be requested to allow discounts on fares for those attending the Congress.

Every effort will be made to secure hotel accommodations in Chicago, provided reservations are made long enough in advance.

The registration fee for the Pan-American Congress will be $5.

Those wishing to attend the Congress are requested to communicate immediately with the Secretary. Titles for papers or motion picture films in any of the four official languages, Spanish, Portuguese, French and English, are solicited by the Program Committee.

CHEVALIER L. JACKSON, Secretary,
Pan-American Congress of Oto-Rhino-Laryngology
and Broncho-Esophagology
255 South 17th Street
Philadelphia 3, Pa., U. S. A.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

The fourth meeting of the Central Illinois Society of Ophthalmology and Otolaryngology was held at the Hotel Orlando in Decatur, Ill., on April 27 and 28, 1946. The following papers were presented:

Saturday, April 27: 12:30 p. m.–1 p. m., "Perforating Ocular Injuries," Dr. Perry E. Duncan. 1 p. m.–3 p. m., "A Full Plastic Eye Implant" and "Exophthalmos," Dr. A. D. Ruedemann. 3:45 p. m.–5:45 p. m., "Diagnosis and Treatment of Ménière's Disease" and "Selection of Cases for the Fenestration Operation in Otosclerosis," Dr. Henry L. Williams.

Sunday, April 28: 10 a. m.–10:30 a. m., "Treatment of External Otitis," Dr. Meredith Ostrom. 10:30 a. m.–11:45 a. m., "Headaches from the Standpoint of the Otolaryngologist," Dr. H. L. Williams. 11:45 a. m.–1 p. m., "Treatment of Lesions of the Cornea," Dr. A. D. Ruedemann.

At the business meeting at 1 p. m., April 28, Dr. Stuart Broadwell Jr. was elected president for 1946; Dr. Walter Stevenson, president elect; Dr. Clarence E. McClelland, vice president, and Dr. William F. Hubble, secretary-treasurer.

Abstracts from Current Literature

Ear

THE RAMSAY HUNT SYNDROME. NORMAN R. SHULACK and MILTON H. KIBBE, J. Nerv. & Ment. Dis. **101**:9 (Jan.) 1945.

The syndrome of herpes zoster auricularis with facial palsy and auditory symptoms was first described by Ramsay Hunt in 1907 and has been infrequently reported since. The authors describe the case of a 27 year old soldier who was hospitalized because of vertigo, inability to close the right eye and pain in the right ear. Examination revealed right-sided facial palsy of peripheral type, redness of the right concha, nerve deafness in the right ear, hypalgesia and hypesthesia of the right side of the face and absence of the right corneal reflex. The next day a herpetic eruption appeared on the concave surface of the right concha. Spinal tap on the eleventh day revealed that the fluid was under normal pressure, with a count of 44 cells per cubic millimeter, of which 95 per cent were lymphocytes. Improvement was progressive, and by the thirty-fourth day the patient had completely recovered.

The authors believe that this case lends support to the view that herpes zoster is a trophic expression of fairly localized inflammation of the central nervous system.

CHODOFF, Langley Field, Va. [ARCH. NEUROL. & PSYCHIAT.]

INHIBITION OF ACTIVITY IN SINGLE AUDITORY NERVE FIBERS BY ACOUSTIC STIMULATION. ROBERT GALAMBOS and HALLOWELL DAVIS, J. Neurophysiol. **7**:287 (Sept.) 1944.

Galambos and Davis studied by means of microelectrodes the nerve impulses in a single auditory nerve fiber. The spontaneous discharges which occur in silence in some fibers can be stopped by certain tones or noises. Inhibitory and excitatory tones for each fiber fall into definite frequency ranges, but there is no common relation between fibers as to the relationship of these inhibitory and excitatory frequency ranges. The discharge excited by an adequate tone can be reduced or abolished by simultaneous presentation of a second tone, and the inhibitory area may encroach on and overlap the response area. The inhibitory effect of low tones on activity aroused by high tones is more widespread than the inhibitory influence exerted by high tones on the activity elicited by low tones. The mechanism of the inhibition is unknown. Factors referable to the middle and the inner ear have been excluded. The authors suggest that nerve fibers underlying the organ of Corti play a role. The function of the inhibition is obscure, but it seems probable that it plays a role in the phenomenon of masking.

FORSTER, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

SOME ORIENTATING REMARKS ON TUNING FORKS AND AUDIOMETERS AND ON THE REGISTRATION OF DEFECTS OF HEARING. S. H. MYGIND, Acta oto-laryng. **33**:1 (Jan.-Feb.) 1945.

The old rule that defects of the sound-conducting mechanism are characterized by clearcut or preponderant low tone deafness and defects of the sound perception mechanism by high tone deafness applied only to tests made with tuning forks and the monochord. In audiometry the findings for the sound-conducting mechanism practically never follow this rule. In cases of severe interference, such as otosclerosis, the audiometric curve forms a horizontal line; i. e., the loss of hearing

is equally great in the low and in the high tone ranges. In cases of relatively mild interference—for instance, tubal stenosis and impacted cerumen—the curve even declines to the right; i. e., there is apparently a high tone deafness, so that this curve is more suggestive of an involvement of the perceptive mechanism.

In order to understand these audiograms one must first establish that the relation between the physical energy of the source of the sound and the biologic reaction, namely, the subjective loudness, is not the same for all frequencies. It is for this reason, for instance, that in the radio one cannot employ the same amplifier for low tones as for high tones, and that at a concert one may shut out the frequencies of the deep-toned instruments by putting one's fingers in one's ears, whereas those of the high-toned instruments come through almost unchanged. With the same increase in physical energy at the source of the sound the increase in the subjective loudness of the sound is about twenty times as great at the 50 decibel level as at the 1,000 decibel level. At lower frequencies the disproportion is even greater; so the same number of physical decibels at the source of the sound may correspond to widely different values in the biologic effect as far as subjective loudness is concerned. To give a hearing defect in decibels as has been customary hitherto is therefore quite misleading.

On the basis of Fletcher's and Munson's "equal loudness curve" it is now practicable to set up a scheme for converting decibels into sones. By converting the audiometric result in this way one obtains audiograms which in all lesions of the sound-conductive apparatus show a clearcut low tone deafness which is in harmony with the results obtained by the use of tuning forks as well as with the sensations of the patients themselves. In severe defects of the sound-perceptive mechanism the low tone deafness becomes more conspicuous than before.

The accuracy of the tuning fork and the monochord method is no greater than that of audiometry. Each of the two methods has its drawbacks and its advantages, so that neither of them can be discarded.

Pharynx

EFFECTIVENESS OF PENICILLIN IN THE TREATMENT OF VINCENT'S ANGINA. BERNARD M. SCHWARTZ, J. A. M. A. **128**:704 (July 7) 1945.

In 14 patients Vincent's angina, demonstrated by clinical and laboratory data, responded well to penicillin administered intramuscularly. The usual dosage was 100,000 units given as 20,000 unit doses at three hour intervals. Less was required for mild and more (200,000 units) for severe infections. Subjective improvement and smears negative for the organisms were obtained rapidly, usually within twenty-four hours. The exudate disappeared in from one to ten days.

BAIRD, Wauwatosa, Wis. [AM. J. DIS. CHILD.]

A CASE OF LUDWIG'S ANGINA. V. LATRAVERSE, Union méd. du Canada **74**:28 (Jan.) 1945.

A girl of 16 years had submaxillary swelling and dysphagia for two months. Suddenly the symptoms became more acute, and difficulty in breathing developed. She was given penicillin, 20,000 units intravenously, together with 800 cc. of a 5 per cent solution of dextrose in isotonic solution of sodium chloride. Laryngoscopy showed compression of the airway in the epiglottic area, with some inflammation of the supralaryngeal structures. A Mayo tube was placed in the pharynx, but oxygenation was not sufficient until a bronchoscope was introduced. With the patient under anesthesia induced by pentothal sodium, the abscess was opened and drained. Tracheotomy was also done. Penicillin was given for four days. Sulfadiazine and liquid foods were given through a stomach tube. Recovery was prompt and complete.

DAFFINEE, Melrose, Mass. [AM. J. DIS. CHILD.]

Nose

COLLOIDAL NASAL TAMPONADES. GEORGE D. WOLF, J. A. M. A. **130**:273 (Feb. 2) 1946.

Wolf states that there is no other type of nasal therapeusis so empiric and yet so widely used as that of nasal tamponades saturated with a solution of mild protein silver. He rightly refers to some bizarre claims that have been made for these packs as relieving or curing any and all nasal disturbances, from "catarrh" to empyema of the antrum, and even to cure of asthma and some ocular infections.

He comments on the views of Dowling, Voorhees, Dean, Williams and Mousel and Gable, the proponents, and the views of Nadler, Bowers, Furstenberg, Swain, Mithoefer, Walsh and Cannon, the opponents.

Further discussions include the history of colloidal silver, the pharmacology thereof, experimental studies and unfavorable effects (the author emphasizing Bryant's point, the danger of argyria, and Criep's, allergy). This fine article continues on with the physiology of the nose and the indications for and against tamponage. In conclusion the author states that the colloidal silver tampons are limited in their local effects, that no particular technic will produce superior results, that the action of colloidal silver at best is probably due to its free silver ions, that some ciliary damage may be produced when the nose is tightly packed with tampons, that patients should not be tamponaded for a period of months or years, that palliative care rather than a correct diagnosis may be the result, that occasionally the "catarrh" in plethoric persons may be relieved, that allergy may result and finally that nasal tamponade as a routine method for chronic sinusitis has no physiologic or pharmacologic basis for either the rhinologist or the general practitioner.

GORDON, Philadelphia.

Miscellaneous

THE USE OF PRODUCTS OF FIBRINOGEN AND THROMBIN IN OTOLARYNGOLOGY. H. P. SCHENCK, California & West. Med. **63**:80 (Aug.) 1945.

Fibrin foam with thrombin is considered by Schenck to be of considerable value as a hemostatic agent in operations on ear and throat. Where fibrin foam products are not suitable, a solution of fibrinogen and thrombin can be substituted. This preparation has been used in skin grafting. It is effective in the control of nasal hemorrhage in patients with leukemia and other blood dyscrasias. The mucous surfaces are either sprayed with the solution, or gauze packing impregnated with it can be used. Fibrin film is a plasma plastic and can be used in repair of septal perforations. It is strong, translucent and pliable. It is suitable for introducing between undermined tissues and additional sheets of the films can be applied on either side of a defect. Its use is less practicable in the case of a large tissue defect.

SELTZER, Philadelphia.

ESOPHAGEAL VARICES. C. O. PATTERSON and M. O. ROUSE, J. A. M. A. **130**:384 (Feb. 16) 1946.

It is well known that recurring massive hemorrhage, ultimately resulting in death, often occurs in patients who have untreated esophageal varices As seen by roentgen and esophagoscopic examination, the bulbous veins projecting into the esophageal lumen are daily subject to trauma from the swallowing of boluses of food. They may ulcerate and rupture, resulting in massive loss of blood. Esophageal varices appear to serve no useful purpose that cannot be served by other and nonvulnerable anastomoses between the portal and the systemic venous circulations.

The authors state that it is their experience that obliteration of these veins results in no appreciable unfavorable effects and that clinical improvement occurs soon after the loss of blood from the ruptured varix is prevented.

The authors injected esophageal varices with a 2.5 or a 5 per cent solution of sodium morrhuate. They report 8 interesting cases, commenting on them with suggestions that are instructive and worth trying. They state that to direct inspection through the esophagoscope esophageal varices in some instances appear large enough to occlude the esophagus. Contraindications to esophagoscopy should always be borne in mind. The ultimate evaluation of the injection of the sclerosing solutions will have to await time and careful observation of these patients. The results so far noted by the authors seem to justify the procedure.

GORDON, Philadelphia.

PENICILLIN TREATMENT OF ORAL INFLAMMATIONS IN CHILDHOOD. M. B. MARKS, J. Pediat. **26**:582 (June) 1945.

The usual treatment of thrush, Plaut-Vincent infection and herpetic stomatitis —applications of gentian violet medicinal and irrigations with boric acid and peroxide and with sodium perborate and glycerite of boroglycerin—suffices in most cases. However, for severe infections the treatment is long and tedious and is trying both to the pediatrician and to the patient. In these cases the use of penicillin, topical and intramuscular, is invaluable because of the rapidity with which it brings about amelioration of symptoms. From 10,000 to 20,000 units of penicillin, depending on the age of the child and the severity of the infection, is injected intramuscularly every three hours. For small infants a total dose of 40,000 to 50,000 units is all that is necessary. For older children the total dose is usually 100,000 units. A greater amount may be employed when it is thought necessary, but in the author's experience the total dose stated seems to be adequate.

For young infants or for older children when it is not desirable to carry out the injection technic penicillin may be used topically in a concentration of 250 units per cubic centimeter. In this method the solution is applied to the affected gums and buccal surfaces with swabs and loose cotton packing. Although the results are a little slower than with the intramuscular route, they are as good, and certainly the method is more effective than the former procedures of using dyes, oxidizing reagents and mild and strong antiseptics.

For particularly severe infections a combination of both the topical and the injection technic may be carried out. The intramuscular route should be preferred. It is seldom that more than four or five deep injections are required, and these can be given within a period of twelve to fifteen hours.

From his experience in treating a number of infants and children with the oral manifestations of thrush, Plaut-Vincent infection and herpetic stomatitis, Marks is convinced that penicillin now supersedes all hitherto employed remedies as being the most reliable and effective. AUTHOR'S ABSTRACT. [AM. J. DIS. CHILD.]

SPEECH DISORDERS IN WORLD WAR II: III. DYSARTHRIA. WILLIAM G. PEACHER, J. Speech Disorders **10**:287, 1945.

At the McGuire General Hospital, Richmond, Va., 25.31 per cent of all patients studied with speech defects had dysarthria; 100 soldiers have thus far been observed with this complaint. In 69 per cent of the cases the difficulty represented a lesion of the peripheral nervous system, and in 86.95 per cent of the latter it was due to a pathologic involvement of the facial nerve. When the symptom is due to a supratentorial lesion, it is usually associated with other neurologic signs. Rehabilitation is usually indicated in involvements of the central nervous system, but only occasionally in peripheral lesions. Return to duty is usually possible in the absence of other disqualifying neurologic residuals.

PALMER, Wichita, Kan.

INFANT SPEECH SOUNDS AND INTELLIGENCE. ORVIS C. IRWIN and HAN PIAO CHEN, J. Speech Disorders **10**:293, 1945.

A statistical analysis was made of the scores from the application of the Kuhlman test and the Chen index of speech development to 19 children from 1 to 6 months

of age, 22 from 7 to 12 months, 32 from 13 to 18 months and 18 from 19 to 24 months. It was found that during the first two years of life the scores on speech sound development are independent of intelligence test scores. Chen's differential method of scoring the elements of premeaningful infant speech may be considered another useful index in estimating the general development of infants.

PALMER, Wichita, Kan.

CONTROL OF ATHETOTIC TREMORS BY SOUND STIMULI. MARTIN F. PALMER and LOUIS E. ZERBE, J. Speech Disorders **10**:303, 1945.

A youth with cerebral palsy, presenting a typical athetotic tremor of the right index finger, was subjected to a series of 126 experiments of varying lengths (mainly auditory) under controlled conditions. It was possible to increase and control the severity, the rate and the stability of the tremor by means of stimuli. When an increase had occurred, it was discovered that sudden cessation of the stimulus (rhythmic, arrhythmic, musical, not musical, etc.) produced remission of the tremor for a considerable length of time. An instantaneous loud sound, produced as an integral part of the experimental sequence, gave the best result. The remission following the experimental series lasted for six weeks.

PALMER, Wichita, Kan.

PRIMARY SUTURE OF SIMPLE MASTOID WOUNDS. L. F. JOHNSON and PHILIP S. SPENCE JR., New England J. Med. **231**:116 (July 27) 1944.

Primary closure of 44 postaural mastoidectomy wounds is reported. This method of treatment has been made possible by the sulfonamide drugs, which when used locally reach high concentration and virtually sterilize the wound. More than half the cases were those of mastoiditis complicating scarlet fever. In these it was possible to reduce the period of hospitalization from fifty-two days to twenty-seven days on the average. Patients without scarlet fever went home with dry ears, and the postaural wounds healed in an average time of fifteen days.

In all of 12 private cases the treatment was successful, the patients being discharged with dry ears and healed postaural wounds. Primary cures were effected for 6 of 8 patients treated by the hospital staff and for 19 of 25 patients with contagious disease. Primary suture requires close attention to the exenteration of all mastoid cells and to complete hemostasis.

In the early cases of this series patients were kept in the hospital longer than absolutely necessary in order to observe the effects of primary suture. Those admitted later, generally speaking, were allowed to go home in fewer days. Doubtless, results can be improved with standardization of operative technic. No serious complications were seen in primary closure, even in the cases in which the sinus or the dura was exposed. The temperature promptly returned to normal after every operation, and the authors observed no intracranial complications. In some cases the postaural wound ruptured for a short distance, but unless it became necessary to do a complete revision, all these wounds healed spontaneously in a shorter time than was required by the earlier method. Sutures were removed on about the fifth postoperative day. AUTHORS' SUMMARY. [AM. J. DIS. CHILD.]

DYNAMIC FACTORS IN THE MOTOR-KINESTHETIC METHOD OF SPEECH CORRECTION. W. ARTHUR CABLE, Quart. J. Speech **31**:350, 1945.

Cable studied the work of Mrs. Edna Hill Young during the second term of the 1943 summer session of the University of Denver Speech Clinic. The following conclusions were reached: 1. The motor-kinesthetic method of developing and correcting speech consists primarily of dynamic concepts, principles and procedures. 2. Neuromuscular learning is at the vortex of the motor-kinesthetic method. 3. The motor-kinesthetic method of correction is centered on muscle movement and allied dynamic factors. 4. The dynamic factor of energy, in terms of muscular force, is

recognized and utilized as an essential. 5. Those who learn this method are taught to recognize and build toward the integration of the total organism as an instrument of speech. 6. The dynamic content of this method appears to be the primary cause of its superiority over the visual-auditory method. 7. The employment of motivation by the correctionist or the clinician is vital. 8. The method under consideration is a striking application of the educational principle that all learning should be acquired through activity of the learner. Two illustrative cases are presented.

PALMER, Wichita, Kan.

THE SPASTIC'S SPEECH SITUATION. STELLA MCKIBBEN, Quart. J. Speech **31**:358, 1945.

In the lives of persons with cerebral palsy, social environment is a great influence for either good or evil because of its effect on the reactions of nerves and muscles. Specialists believe that they know the importance of social environment, but they often do not take the time to go into a detailed consideration of it in each case. Parents usually believe that the spastic child is shockingly ill and consult many physicians, thus building up abnormal concepts, and the child thus goes through a disastrous environment, which has a direct effect on his condition. Any one working with spastic children should understand the importance of environment and maintain an understanding attitude in helping them to express themselves orally and otherwise.

PALMER, Wichita, Kan.

THE SEMANTIC ASPECTS OF STUTTERING IN NON-STUTTERERS: ADDITIONAL DATA. JESSE J. VILLARREAL, Quart. J. Speech **31**:477, 1945.

Villarreal gave 154 males and 117 females—all normal speakers—the following questionnaire: 1. Did you ever have a stuttering defect of speech? 2. Did any one ever call you a stutterer? 3. Did any one ever say you were stuttering? 4. Do you think you ever said anything stutteringly? 5. Do you think you have a habit of stuttering? 6. Did you ever call yourself a stutterer?

The collected data in general reproduced those originally reported by Voelker. Fourteen per cent had had a stuttering defect of speech; 6.7 per cent had been called stutterers; 29.1 per cent had been said to be stuttering; 76 per cent thought they had spoken stutteringly; 1.8 per cent thought they still had the habit; 9.9 per cent had called themselves stutterers. The data for the most part are sex differentiated. Almost twice as many males, for example, have been said to be stuttering as females.

PALMER, Wichita, Kan.

CORRECTION

In the article by Major Joseph H. Hersh entitled "Plastic Repair of a Large Alveolar-Antral Fistula" in the February issue (ARCH. OTOLARYNG. **43**:141, 1946), the first paragraph at the top of page 142 should read: Step 2. A gingivobuccal flap was elevated (indicated as *B* in figure 1). This had been previously prepared as a delayed and diverging flap to assure adequate circulation.

In the paragraphs beginning "Step 3" and "Step 5," the words "The buccal flap" should read: The gingivobuccal flap.

Directory of Otolaryngologic Societies *

INTERNATIONAL

First Pan-American Congress of Oto-Rhino-Laryngology and Bronchoesophagology

Predident: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Chevalier L. Jackson, 255 S. 17th St., Philadelphia 3.
Place: Palmer House, Chicago. Time: Oct. 17-19, 1946.

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. Louis H. Clerf, 1530 Locust St., Philadelphia.
Secretary: Dr. Fletcher D. Woodward, 104 E. Market St., Charlottesville, Va.
Place: San Francisco. Time: July 1-5, 1946.

American Academy of Ophthalmology and Otolaryngology

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.
Place: Palmer House, Chicago. Time: Oct. 13-18, 1946.

American Broncho-Esophagological Association

President: Dr. Robert M. Lukens, 1923 Spruce St., Philadelphia.
Secretary: Dr. Paul Holinger, 700 N. Michigan Ave., Chicago 11.

American Laryngological Association

President: Dr. Frank R. Spencer, Physicians Bldg., Boulder, Colo.
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American Laryngological, Rhinological and Otological Society, Inc.

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Secretary. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y.

SECTIONS:

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Southern.—Chairman: Dr. Walter T. Hotchkiss, 541 Lincoln Rd., Miami Beach, Fla.
Middle.—Chairman: Dr. Oliver E. Van Alyea, 135 S. La Salle St., Chicago.
Western.—Chairman: Dr. Colby Hall, 1136 W. 6th St., Los Angeles, Calif.

American Otological Society

President: Dr. William E. Grove, 324 E. Wisconsin Ave., Milwaukee, Wis.
Secretary: Dr. Gordon D. Hoople, 713 E. Genesee St., Syracuse, N. Y.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Inc.

President: Dr. Alfred Schattner, 115 E. 61st St., New York.
Secretary: Dr. Norman N. Smith, 291 Whitney Ave., New Haven, Conn.
Place: New York: Time: Nov. 14, 1946.

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.

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